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ROLE OF PEDIATRICIAN IN PHYSICAL FITNESS OF YOUTH

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A comparison of American with European school children as to physical fitness was made in 1953 by applying the six basic Kraus-Weber tests to 4,458 children in this country and about 3,000 children in Italy and Austria. These tests evaluate the strength of the psoas, the lower abdominal muscles, and the lower and upper back muscles, as well as flexibility of the back. The results showed the physical inferiority of American children in physical performance, and subsequent findings indicate that the fitness level of the general public has been falling steadily even while the performance of selected star athletes has improved. The tendency has been for the number of active participants in athletics to decrease while the number of people watching by television and applauding comfortably from armchairs has increased. The pediatrician can do much to remedy this, for he is the family's best friend. He should help the child realize early in life that a flexible, strong body is vitally important.

BY THE USE of the term "pediatrician" in the title of my paper I mean to refer not only to those with specialty training in the care of infants and children but to all physicians who care for children. The pediatrician is the first friend an infant has, apart, of course, from his parents. And since parents turn to the physician for guidance in raising a healthy baby and when sickness strikes, one could say that a pediatrician is the family's best friend. The pediatrician is the first to meet the family medically and to introduce good health routines. He is the first to schedule and interpret the series of immunizations that start today in infancy and play an increasingly important role in getting the baby safely up to and through the health hazards of childhood.

The pediatrician with a knowing heart can wield a lifelong influence on the healthy development of the child. He can and should contribute to family understanding of the needs of the infant, and shape his growth as he progresses into childhood and on toward adulthood. Basic health principles established early guide an individual's growth and development. Our society gives the pediatrician a chance to apply the modern concept of total care. The pediatrician is the first to recognize the well baby as an entity, and he understands that physical fitness is closely related to the mental and emotional development of the child entrusted to his guidance. Not only does physical fitness represent an important segment of child development but it increases in significance as the child progresses on to maturity.

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Read before the Section on Physical Medicine at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

As we look about us today, mindful of how seriously we took our responsibilities, many of us find cause for more amazement than pride in some of the children we remember as our healthy infant patients. Too often we see deterioration instead of development, young bodies, once firm and flexible, beginning to go slack and soft. We hear about too many backaches, and we are appalled. What has gone wrong? We realize, sometimes too late, that physical fitness is not a static condition. It can be established by simple, repeated routines but those routines must be expanded and maintained.

Comparative Fitness Tests

In 1953, health leaders and school authorities were shocked into active concern about the comparative physical development of American and European children.[2] Most pediatricians may recall the facts if not the specific data. Six fairly simple, basic tests of physical fitness were given to 4,458 normal American school children. Known as Kraus-

SPORTS ILLUSTRATED
HOW TO KEEP FIT
NATIONAL YOUTH FITNESS WEEK
U.S. News & World Report
WHY INFLATION SWEEPS THE WORLD
Is American Youth PHYSICALLY FIT?
FITNESS FOR YOUTH

Fig. 1.—Montage of part of large number of articles appearing in press on physical fitness of youth.

Weber tests, these included tests for abdominal muscles, lower back muscles, upper back muscles, and flexibility of back and hamstrings.[3] Similar tests were given to about 3,000 European school children, primarily in Italy and Austria.[4] At every age, from 6 to 16, the American group proved less muscular than the European group; 57.8% of the American children failed to pass, compared with less than 8.17% of the Europeans.

Results of these Kraus-Weber tests came as a shock to most Americans, who take their physical superiority somewhat for granted, particularly in the field of sports. The President appointed a special committee to "investigate." A rash of newspaper and magazine articles analyzed, deplored, and questioned the situation (fig. 1). Were we becoming a nation of "push button softies?" Were our high standards of living responsible for the physical deterioration of our youth?

There was reason for the agitation, and there is still a point behind the questions. In March, 1958, the President's Council on Youth Fitness again was charged with alerting the nation to the potential danger toward which many symptoms increasingly point. Many who have followed these special conferences have been disappointed at the lack of concrete action by these gatherings of large numbers of highly talented people.

European children do not have the benefits of our highly mechanized society, and this seems to underscore the major difference between the physical fitness of the two groups studied. They walk where we ride. They do not use—to the extent we do—cars, school buses, elevators, or other of our great laborsaving devices. Their recreation is largely based on the active use of their own bodies; they are sports participants, where we are sports spectators. Their daily routine of living keeps them more active physically than does ours, and this activity builds muscles, develops strength, insures flexibility and fitness. We live better, eat better, have better medical care, and have more time for rest and leisure, but are these really the blessings they appear to be?

Since 1953, when these studies were first called to national attention, the situation on the American scene seems to have become worse rather than better. Television has taken tighter hold on both children and adults. In too many homes the greatest physical activity seems to consist in switching channels or moving from the television set to the kitchen to pick up a snack during commercials. Lack of physical activity has become an increased menace to the health and development of our youth.

A few years ago the following statement appeared in a report of the National Conference on Physical Education for Children of Elementary School Age: "Every child needs sufficient muscular strength to maintain good posture at rest and in motion and to do with vigorous physical activity. Strength coupled with a flexible body gives him ability to move quickly and effectively. He needs the stamina and endurance that depend on well developed heart and lungs to persist in work and play without undue fatigue. Strength, agility and endurance come from play that is long and intense enough to tax the body beyond the ordinary." [5]

The Lankenau Hospital in Philadelphia held a research conference on "Maturing Man: Growth and Aging" on Oct. 24, 1957. Kaare Rodahl, director of clinical research at the hospital, emphasized the role of physical fitness in longevity: "What a man is able to do at 70 years of age depends largely on what he did at 7."

Pediatricians should evidence greater interest in these two significant statements than they have shown to date. Very often, it is true, the pediatrician is so busy with problems of acute illness and today's numerous immunization procedures that he

may overlook the necessity of encouraging patients to maintain even minimum standards of muscular fitness, but it is early interest in physical fitness that stimulates a child's desire to develop muscular strength, agility, and flexibility. If his interest lags, the child can all too easily and quickly drop below the minimum standard of fitness required for general good health and well-being. We've all seen it happen too often. Seeking medical means to alleviate muscular pains and backaches, we have found their origin not in orthopedic difficulties but in lack of sufficient exercise.[10]

Morris and Heady [6] and other English authorities,[7] as well as Benton and Rusk,[8] point to a definite relation between physical activity and coronary heart disease in middle age by reviewing employment data on cardiac cases. They have found that the disease is not so severe in physically active workers, who tend more to develop angina pectoris and other relatively benign forms, and have lower mortality. Pomeroy and White, in their study of former Harvard football players, found that those who maintained some degree of regular exercise were less prone to develop coronary heart disease and that "no individual in [their] study who maintained a heavy exercise program happened to develop coronary heart disease." [9]

Exercise and Deficiency

Developing the tests for physical fitness that bear his name, Dr. Hans Kraus [10] demonstrated that lack of sufficient exercise blocks off emotional release and decreases muscle strength. City traffic, shrill telephones, and high pressure work combine to keep us in a state of irritation but deny us the necessary physical outlet of release. Impulses inhibited from responding to such outside stimuli can, and do, result in general and local muscle tension. Physical activity, walking, and even stair-climbing, dancing, and other active sports are excellent outlets for these impulses.

There has been criticism of the Kraus-Weber tests from many sources. I do not mean to imply they are the only tests. Certainly some of the more complete physical profiles, such as those designed by the American Association for Health, Physical Education, and Recreation, give a more complete picture of total physical abilities. Almost every school of physical education has its own modification. All these are fine, but they cannot be done in a doctor's office. Kraus never implied that if a child passed his test he was *de facto* free of any medical or surgical impairment, merely that these were simple tests which had been given to large groups of children. Considerable data are available on the results. Failure in one or more of the tests indicates a lack of the minimum strength and flexibility necessary for ordinary living. These tests can be given in an office by a nurse after a short period of explanation. From a medical standpoint they are ideal, because the possibility of producing harm by the tests themselves, even before a physical evaluation, is nil.

Our mechanized, over-convenient life, by reducing muscular activities to a bare minimum, deprives us of the exercise that is necessary to maintain adequate physical fitness. Most of us get along with minimal muscular equipment until such time as a trivial occurrence forces us to exceed the existing limitations of our muscles. When we lift a 30-lb. suitcase, for instance, or stoop to pick up a dropped pencil, the effort may result in acute muscle strain which either improves by itself or causes us to seek some palliative remedy. This strain further reduces the efficiency of our muscles and we go along rather carefully until another strain occurs. Repeated episodes may lead to conditions that actually do stimulate orthopedic difficulties, and prolonged suffering frequently ties in with some emotional instability until finally we are confronted with a well-established illness that comprises not only the physical but also the emotional life of a person.[7]

Kraus showed that systematic muscle training relieves the situation. Patients encouraged to exercise improved rapidly and regained strength and flexibility, but they quickly lost ground if physical activities were reduced or given up. It is his contention that lack of sufficient exercise constitutes a serious deficiency, comparable to vitamin deficiency.

Prevention of this muscular deficiency is, it seems to me, the pediatrician's business. He cannot do it alone, of course, but he can and should play a bigger role in the basic health picture than he does now. His influence on parents, teachers, and others charged with responsibility for children's health can make a sizable dent in the growing problem. At the risk of sounding old-fashioned, I would like to remind you that physical activity was an earnest recommendation, even a prescription, of physicians in past decades. And I would like to suggest that it would not hurt us to borrow from the past and restore physical activity to its proper place of importance in a well-balanced life.

The past relates closely to the present when we review the results of the Kraus-Weber tests. A large number of children originally unable to pass the tests made the grade easily after they resumed regular exercise. Their strength and flexibility increased and their complaints lessened or disappeared, but they lost ground again if their physical activities were reduced or discontinued. This indicates rather obviously that muscle fitness levels can be controlled by exercise. It was noted that more American than European children complained of backache, but it was the effort to determine the source of the loss of flexibility and muscular strength that brought about the comparative study of school children here and abroad.

Of interest is the experience in a parochial school in Scarsdale, N. Y. When 385 children in grades 1 to 8 were tested, 59% of them failed two or more of the tests. For the next six weeks the following program was put in effect: a three-minute drill, three

Fig. 2.—Test of strength of psoas and lower abdominal muscles.

times a day, led by one of the students, and a 30-minute period one day a week of strenuous calisthenics led by one of the mothers. The percentage of failures dropped to 35. This program has been expanded; there are now 10 volunteer mothers giving the program, which includes basic tumbling. This is given in the school cafeteria and the chapel, in a school which has no facilities for a physical-education program.[11]

The Kraus-Weber Tests

Many pediatricians are familiar with these six simple tests. They can easily be included during routine examinations of a patient. After a short period of instruction they could be given or supervised by the nurse. These tests represent basic minimum standards of physical fitness. They were designed to indicate the level of strength and flexibility in certain key muscular groups below which function of the whole body as a healthy organism might be jeopardized. Children whose physical fitness level falls below these minimums should be considered "sick people." They are almost invariably youngsters who bear all the earmarks of stress and who frequently manifest signs of emotional instability.

Tests of Psoas and Lower Abdominal Muscles.—In the first test of the strength of the psoas and lower abdominal muscles (fig. 2), the person being tested is supine, with hands behind neck and legs extended. Instructions are as follows: "Keep your knees straight and lift your feet 10 in. off the table. Keep them there while I count." The count is 10 seconds. If the person tested has not understood your command, he may try to raise his chest when he raises his feet and will need further explanation. Watch for an extremely arched back which may indicate weak abdominal muscles or postural habits contributing to sway back or lordosis. Holding for 10 full seconds is passing and is marked as "10." Anything less is recorded as that part of the 10 seconds that was held, for example, "4" for 4 seconds or "7" for 7 seconds.

In the second test (fig. 3), the person being tested is supine, with hands behind neck. His feet are held down on the table by the examiner. He is instructed as follows: "Keep your hands behind your neck and try to roll up into a sitting position." If the person being tested is unable to perform this movement at first try, it may be because he did not understand the directions. Help him a little and then let him try again. Watch for a "stiff back sit-up." This may indicate that either he has not understood you and needs further explanation with emphasis on "rolling up" or that he has very poor abdominal muscles and is doing most of the work with his psoas. Marking is the same as for the first test.

In the third test (fig. 4), the person being tested is supine, with hands behind neck and knees bent. His feet are held down on the table by the examiner. He is instructed as follows: "Keep your hands behind your neck and try to roll up into a sitting position." The precautions are the same as for the second test, but, as this test is usually more difficult, the tendency toward "stiff back sit-up" will be even more pronounced, and to it is added the tendency to help with one or the other elbows. Marking is exactly the same as for the first two tests.

Tests of Upper Back Muscles.—The next three tests concern the back muscles. In the first test (fig. 5), the person being tested is prone, with a pillow under his abdomen so as to give the body the feeling of being a seesaw, which if weighted at either end would be able to hold the other end in

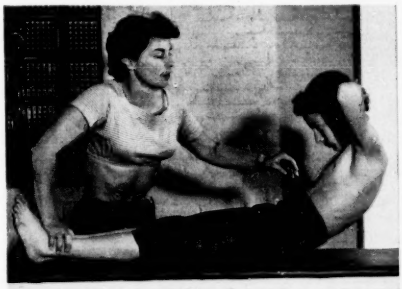

Fig. 3.—Test of strength of abdominal and psoas muscles.

the air. This is most easily accomplished with the following instructions: "Roll over onto your stomach and lift up the middle so that I can slide this pillow under you." (Be sure the pillow is large enough to support him.) "Now, I am going to hold down your feet while you put your hands behind

your neck and raise up your chest, head, and shoulders. Hold them up while I count." The count is 10 seconds.

Do not let the person being tested drop his chest onto the table or rest his elbows. Watch for pronounced muscular development on one side of the

Fig. 4.—Test of strength of abdominal minus psoas muscles.

spine. If this condition is present, the back should be checked from time to time to guard against scoliosis. Holding for 10 full seconds is passing, and is marked as "10." Anything less than 10 seconds is recorded as that part of 10 seconds that was held. For example, a person staying up for 4 seconds would get the mark of "4."

In the second test of the strength of the lower back (fig. 6), the person being tested remains prone over the pillow but removes his hands from behind his neck, places them down on the table, and rests his head on them. The instruction is as follows: "I am going to hold your chest down on the table. Try to lift your legs up but do not bend your knees." There may be a tendency to bend the knees or even to support the legs by keeping the toes on the table. It may be necessary to assist him in the required position. "Now, hold this position while I count 10." Marking is the same for the other tests. The last test is of the length of back and hamstring muscles (fig. 7). The person being tested is standing erect in stockinged or bare feet, hands at his sides. The instruction is as follows: "Put your feet together, keep your knees straight, now lean down slowly and see how close you can come to touching the floor with your finger tips. Stay down as far as you can for a count of three. Do not bounce."

Watch out for bouncing. The furthest point reached without bouncing and held for three counts is the marking point. The examiner should hold the knees of the person being tested in order to prevent any bend. Touch is designated with "T." "Touch" is only given when the floor-touch is held for three counts. Less than "Touch" is marked by the distance in inches between the floor and the finger tips. For example, a person unable to touch the floor by 2 in. would be marked "–2."

Test Results

When the Kraus-Weber tests were first given to American school children we thought that our minimum standards might be too high to be met by the average school child, but the European results indicated that this was not necessarily so. It seemed that our American standard of living was too high. We do not balance our modern mechanized conveniences with a reasonable amount of compensating physical activity. There are not many men left who have drawn water or hewed wood, and as adult physical work becomes less arduous the children's chores become less demanding. As time goes on and new and better laborsaving devices keep being added to the market our general population becomes less and less physically active.

It is somewhat contradictory, therefore, to note that while the fitness level of the general public is steadily falling our specialized teams of selected star athletes are becoming more physically outstanding year by year. We are loud in admiration of their prowess, which we watch and applaud comfortably from our soft armchairs. Increasingly few of us get, or take, if offered the opportunity, much personal physical exercise. As we become ever more urban, the numbers of our sedentary workers increase, while our senses are continuously assaulted by emotionally packed stimuli from radio, television, movies, and world-wide news coverage. Our tensions increase steadily, and our physical exertion, which might help relieve them, as steadily decreases.

Jack Wickstrom, professor and chairman of the division of orthopedic surgery, Tulane University School of Medicine, declared that one of the biggest

Fig. 5.—Test of strength of upper back muscles.

faults of the school system generally is that physical education is merely supervised play. Schools no longer carry out posture exercises and gymnastics.[11b]

Three attitudes have been rather prevalent among pediatricians. One is that, as there may be a real danger in having a child with a physical impairment, particularly of the cardiorespiratory system,

participate beyond his ability in strenuous competitive contact sports, they are against all fitness programs. You will all agree that the first part of any fitness program is a thorough physical examination by the pediatrician, who should advise the child

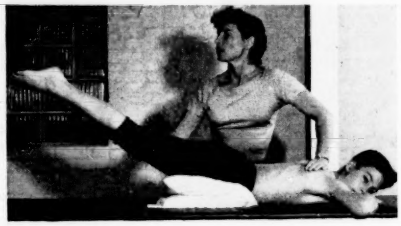

Fig. 6.—Test of strength of lower back.

and his parents as to any limitations in physical activity, and make certain that correctly designed protective equipment is properly worn. It is interesting to note that most of the problems arising from certain Little League programs are caused by adults participating too much in the program.

Second, a few pediatricians have objected to the emphasis on physical fitness by claiming that it segments off a small part of total development, maintaining that there are other aspects of fitness, such as moral and educational. I heartily agree with this, but I feel that any competent pediatrician takes these matters into account in dealing with his patient and family. My chief concern is that the pediatrician play his rightful role in the fitness of youth. Lloyd Appleton, of the physical education department of the United States Military Academy at West Point,[12] has studied the relationship of physical fitness, as determined by the results of the physical aptitude entrance test, to future leadership and to discharge because of psychiatric disability. He found that those falling within the lowest 7% of the group on physical aptitude scores made up the largest number of those discharged for psychiatric reasons and that among those in the top 7% of the group there were no discharges for psychiatric disorders. The highest number of cadet leaders came from the upper 7%.

The third attitude among pediatricians is simply a disinterest in the fitness of youth as regards muscle strength and flexibility. I feel that this attitude can no longer be held, because of the tremendous publicity on and public interest in this problem. The week of June 1-7, 1958, was declared Youth Fitness Week by President Eisenhower. When the new president of the Junior Chamber of Commerce took office in Los Angeles, he stated that the J. C.'s were taking up the problem of the physical fitness of youth as the theme of one of their major programs this year. Anyone who is familiar with the dynamic leadership of this group knows that there will be great activity throughout the United States as a result of their interest in this problem.

Recommendations.—I have three recommendations. First, the pediatrician must take an active role in the physical fitness of American youth. There is a definite problem, with implications of a serious natural deficit, if the present laxity in physical education is allowed to continue. Various lay groups are becoming increasingly active in this field. The pediatrician must stand ready to give the needed advice, counsel, or leadership when necessary. He should emphasize the necessity of taking a complete history and physical examination prior to the child's participation in a fitness or sports program. Second, the pediatrician should encourage the use of the six Kraus-Weber tests as a basic screening device for detecting minimal physical competence. Third, the pediatrician should see that the schools in his area provide at least a minimal program of physical education, preferably of strenuous calisthenics.

Conclusions

The pediatrician should realize that he has responsibility for the mental and emotional care as well as the physical development of the child under his guidance. He impedes the healthy growth and development of the child if he considers physical fitness the special province of the educators and physical instructors. He can help parents inculcate in the child a healthy attitude toward physical activity, help youth groups develop programs of activity that build physical strength and fitness,

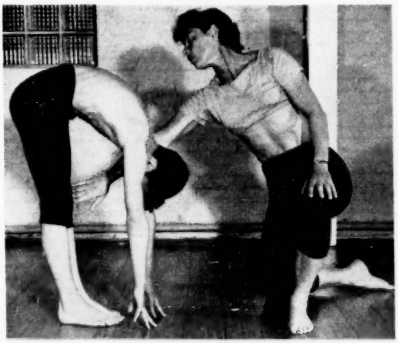

Fig. 7.—Test of length of back and hamstring muscles.

and urge PTA groups to have organized physical training included in all school programs. Physical education programs should be incorporated into the curriculums of all schools, particularly those in crowded city areas where children are already deprived of sufficient physical activity. Finally, the pediatrician should help the child realize early in

life that a flexible, strong body is vitally important for counteracting and combatting physical fatigue, emotional stress, and tension. He should help the child learn that a healthy, physically fit body requires, as do all the worthwhile things in life, hard work and sustained effort.

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REHABILITATION OF FARMERS WITH HEART DISEASE

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The occupational status of 43 men and 3 women with heart disease was studied with reference to the rehabilitative needs and potentialities of farmers. All were employed in agriculture, some with and others without changes or restrictions in their work. The most frequent diagnosis was arteriosclerotic heart disease. When reexamined one to two years later, the group showed no evidence of functional deterioration. A third examination, two to three years after the first, was possible in 30 members of the original group and gave the same result. Two patients had died of second attacks of myocardial infarction that had no apparent relation to the work they did. Methods of estimating functional cardiac capacity and prescribing a safe work load are still unsatisfactory, but this must not deter the physician from giving specific advice to agricultural workers with heart disease. He bases his recommendations not only on figures for energy expenditure and cardiac classification but also on his knowledge of the variables affecting the individual patient.

Increasing efforts are being made to meet the rehabilitation needs of cardiac patients employed in industry. The industrial work evaluation unit admirably serves this group of handicapped people, but similar concern has not been shown for those with cardiovascular disease who are engaged in agricultural occupations. The establishment of formal work evaluation units for rural people is not feasible in most areas for obvious reasons, but medical and social investigation and job analysis are no less urgent for those handicapped for agriculture than for those handicapped for industry.

This report describes the results of a team study of the utilization of community resources for aiding farmers with heart disease to solve their occupational problems. The primary purpose of the demonstration, carried out from 1955 to 1957, was to explore the feasibility of applying the principles and techniques of the industrial work evaluation unit in a rural setting, not for definitive study of a statistically significant group of patients.

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Read before the 31st Scientific Sessions, American Heart Association, San Francisco, Oct. 26, 1958.

Materials and Methods

Our demonstration was carried out in one typical rural Iowa county with a population of 19,550, 8,000 of whom lived on 2,000 farms. Eligibility for participation required employment in agriculture, an age of 16 years or more, a diagnosis of actual or suspected cardiovascular disease sufficiently stable to permit consideration for rehabilitation, and referral by the family physician. A thorough medical evaluation was done at the State University of Iowa Medical Center to establish a diagnosis and assign a functional and therapeutic classification. The county extension director served as the job analyst. A vocational counselor from the State Division of Vocational Rehabilitation substituted for the social worker in the usual work evaluation unit. They both visited all the patients on their farms one or more times.

The drudgery of farming has been greatly reduced through increasing mechanization, but it is estimated that 50% of general farm jobs still are done by hand labor. Even so, energy expenditure can be further reduced by work simplification and thoughtful emphasis on farm management. The specific technique of job analysis used by the county extension director is beyond the scope of this discussion, but his contributions were based on a detailed evaluation of each patient's farm buildings and land, equipment inventory, cropping and livestock practices, and work habits. He assessed the financial status, managerial ability, past performance, and future goals in each case. This type of information must be available before any specific suggestions can be considered for work simplification or managerial changes to reduce the physical stress of farm labor. The physician cannot secure this information; the modernly trained extension agent can. The vocational rehabilitation counselor is an ideal member of such a team, because he is accustomed to dealing with handicapped people and he brings with him the resources of his agency.

The energy costs of farm jobs in most instances exceed those of the majority of industrial jobs. We made use of the data of Passmore and Durnin [1] on the energy costs of selected farm jobs in arriving at suggested changes in work methods. We also used similar data made available to us during the progress of the extensive Farm Cardiac Project at Purdue University,[2] later summarized in a pamphlet by the American Heart Association.[3] It was necessary to consider the factors of weather and peak work loads as well, because they vary greatly with the seasons.

Our goal was to make realistic suggestions to enable physically fit patients to remain in an agricultural occupation if they so desired. If they did not, we offered help in the transition to some other work. Recommendations based on all findings were presented to the patient and his family, at a conference attended by the family physician. Forty-six patients, three of them women, were studied between 1955 and 1957. The value and size of their farms were comparable to the averages for the county and state as a whole. Their educational background was below the average.

Results

The patients' ages ranged from 17 to 77 years. More than half were between 40 and 59 years old. Specifically, 1 was in the second decade, 1 in the third, 7 in the fourth, 14 in the fifth, 11 in the sixth, 8 in the seventh, and 4 in the eighth. The types of heart disease represented are as follows: congenital heart disease (atrial septal defect), 2; rheumatic heart disease, 9, with predominant lesion as mitral stenosis in 1, mitral insufficiency in 3, aortic stenosis in 1, and aortic insufficiency in 4; arteriosclerotic heart disease, 16, with angina pectoris in 4 and healed myocardial infarction in 12; undetermined etiology (manifested by cardiac enlargement and/or history of cardiac failure), 9; hypertensive heart disease, 2; heart disease due to thoracic deformity, 1; neurocirculatory asthenia, 2; and no heart disease, 5.

Functional and Therapeutic Classification of Farmers with Heart Disease[a]

	Results	
	Initial, No.	After 1-2 Yr., No.
No heart disease	5	5
1-A	6	6
1-B	4	4
2-B	9	9
2-C	14	18
2-D	1	0
3-C	1	1
3-D	5	3
4-E	1	0

[a] Classification of the American Heart Association.

The functional and therapeutic classification, shown in the table, indicates that two-thirds of the patients had significantly limiting disease when they came under study: 31 were given the classification of functional class 2 or below. It can be seen also that medical reevaluation one to two years later indicated that the functional status had not deteriorated. In fact, four patients, initially classified as being below class 2-C, had improved.

A follow-up study, directed by Dr. William E. Connor, was completed in August, 1958, in 32 of the 46 patients two to three years after they joined the group. Two men who had had myocardial infarction died from second attacks, but there was no apparent relationship with the limited work they did. There has been no evidence of aggravation of the cardiac disease in the remaining 30 patients.

The results from this method for dealing with the occupational problems of the group do not require detailed description. In summary, they are as follows for 46 subjects: (1) farm without specific changes, 11 (5 without heart disease and 6 in class 1-A); (2) farm by specific use of outlined work simplification measures and changes in farm

management, 10 (4 in class 1-B and 6 in class 2); (3) farm by major changes in farm operation, 2 (both in class 3); (4) retain farm interests by entering into or formalizing existing partnership or lease arrangements to shift major work loads, 7 (5 in class 2, 1 in class 3, and 1 in class 4); (5) rehabilitation by surgery for mitral stenosis, 1 (in class 2); (6) farm temporarily by use of family or hired help to gain time for maximum social security benefits (social security participation for farmers began in 1955), 3 (1 in class 2 and 2 in class 3); (7) discontinue farming and seek more sedentary work, 5 (4 in class 2 and 1 in class 3); (8) retire because of age, disability, and financial status, 5 (all in class 2); and (9) restrict activity to housework and introduce work simplification measures in the home, 2 (both women, both in class 2).

We considered more than energy expenditure and functional cardiac classification in recommending these dispositions. These people possessed all the variables common to human beings generally. Compliance with the advice was excellent.

Comment

This team approach and these techniques are feasible in helping farmers with heart disease to solve their occupational problems. Patient, family, and physician cooperated excellently. The results indicate that the demonstration was medically safe and agriculturally sound. Details of the application of such a multidisciplinary approach will vary with local circumstances, but the results of this demonstration indicate that here, at least, is one practical way to deal with an unmet rehabilitative need. Physicians should not delay giving specific advice to agricultural workers with heart disease who find it necessary to limit their activity just because further refinement in the accuracy of estimating functional cardiac capacity and relating it to the energy expenditure of a safe work load is needed. The physician is the key to the problem. He must bring the patient, the extension agent, and the vocational counselor together. Our experience demonstrates that farmers ask the extension agent for help in solving many of their agricultural problems but the partially disabled are not accustomed to seek specific advice for planning a safe work program. Medical guidance of the kind we have demonstrated will help adjust the farmer to his work and improve his opportunity for health.

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LATE SEQUELAE OF SADDLE BLOCK ANESTHESIA IN OBSTETRICS

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Evidence of neurological damage attributable to saddle block anesthesia was sought in the records of 3,147 obstetric patients who received this type of anesthesia in 1946-1951. Careful long-term follow-up was possible in 1,077 patients. Only six of these had findings that might be related to the anesthesia. These findings were usually altered reflexes, sensory changes in the legs, headaches, and dizziness. No major sequelae were found. In this series of patients the slight disadvantages of saddle block anesthesia were far outweighed by its advantages, especially its effectiveness, safety, and acceptance by patients and physicians.

Prior to 1946, several authors [1] described a technique of spinal anesthesia for relief of pain in labor and delivery, with a hyperbaric solution of dibucaine (Nupercaine) hydrochloride which they called "saddle block anesthesia." Since that time, saddle block anesthesia has become increasingly popular in the field of obstetrics. This method offers advantages to the mother, infant, nursing staff, and physician. There must be some merit in any anesthesia which is as popular as saddle block anesthesia has apparently become, as more than 200,000 obstetric cases with saddle block anesthesia have been reported in the literature since 1946.

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On the other hand, there have appeared in both the obstetric and neurological literature certain unfavorable reports on late neurological complications after saddle block anesthesia. Our enthusiasm for this type of anesthesia must then be tempered if acute or late neurological sequelae develop in significant numbers. The complications after saddle block anesthesia may be acute or immediate, such as hypotension, postanesthetic headache, meningismus, and aseptic meningitis, or late neurological complications represented by chronic headaches, paresthesias, and transient or permanent paralysis.

Review of Literature

In 29,484 cases reported in the literature, there were no major sequelae due to saddle block anesthesia. Seegar and Devlin[2] reported 5,250 cases in seven years at St. Agnes Hospital, Baltimore. Follow-up of the patients proved difficult, but none of the physicians reported serious sequelae or mortality resulting from the saddle block anesthesia. Hospital records showed no mortality or paralysis, transient or permanent. They concluded, "We believe that paralysis from saddle block anesthesia is rare, and that until better obstetric anesthesia is offered, it is far safer than inhalation and more satisfactory than local anesthesia."

Sadove and Levin[3] reported 10,000 patients delivered by saddle block anesthesia without permanent paralysis, but they do not mention the length of time of their follow-up. Reed,[4] reporting 174 cases of cesarean section done with the patient under spinal anesthesia says, "There have been no neurologic complications. Specifically, no case of arachnoiditis has developed in our cases." Makepeace[5] was able to follow 1,606 out of 1,840 patients by letter, asking them to come for examination. Only 375 responded. These represented 425 spinal anesthesias. Only one patient had any neurological symptoms, having had meningismus attributed by one consultant to drug sensitivity. Two other patients complained of less severe degrees of transitory meningismus. Makepeace feels that it is reasonable to presume that no damage due to the anesthetic was found in the entire group, as none existed in the group which returned for examination.

Stanley[6] reported 1,000 cases of saddle block anesthesia without any permanent paralysis. Conti and Natali[7] also reported 2,607 cases of saddle block anesthesia with no known neurological sequelae. Dripps and Vandam,[8] in 1954, reported 10,098 spinal anesthesias given on their surgical service. There were no instances of incapacitating neurological disease, although headaches had occurred in 15% of the females. The few immediate neurological complications in their series disappeared within a few weeks, the longest lasting six months.

On the other hand, several highly unfavorable reports have appeared in the literature implicating saddle block anesthesia in late major neurological sequelae (29 incidents in more than 22,000 cases). So critical have these been that serious doubt as to the safety of this agent has been raised.

Nicholson and Eversole[9] found five patients with major neurological sequelae in 21,000 cases of saddle block anesthesia given for general surgical procedures. Kennedy and co-workers[10] reported 12 patients with grave paralysis admitted to Bellevue Hospital after spinal anesthesia. They conclude that "Paralysis below the waist is too high a price for a patient to pay in order that the surgeon should have a fine, relaxed field of operation," and again that "This anesthesia should be reserved for those patients unable to accept a local or general anesthesia."

Bergner and associates[11] of the University of Tennessee reported six cases of paralysis after saddle block anesthesia occurring during 1949 and 1950. Rosenbaum and co-workers[12] at St. Louis University, in 1952, reported 6 cases of adhesive arachnoiditis in 1,772 patients who had been given heavy dibucaine saddle block anesthesia, also during 1949 and 1950. Paralysis had developed three months to four years after the anesthesia. They were able to follow up 358 of the 1,772 patients. They state in their conclusions that "Spinal anesthesia is too dangerous to justify its use in the un-complicated obstetrical cases."

Minnitt and Gillies[13] wrote "To say that one has not seen complications is only half an answer, because one has probably not looked for them." Babcock,[14] however, says that the dangers of saddle block anesthesia remain largely with the user, rather than the drug and the technique employed.

Results of Neurological Examination at Arkansas Hospital

Our interest in late sequelae of saddle block anesthesia was stimulated by these reports in the literature. We had not noted any serious acute complications, but it was felt that some of the late sequelae might have been missed because patients had not been followed up neurologically for long periods of time. Consequently, we undertook a survey of all patients who had received saddle block anesthesia five or more years ago (Jan. 1, 1946, through Dec. 31, 1951); consequently, some of the patients were examined 10 years after their first spinal anesthesia.

Saddle block anesthesia, primarily with use of hyperbaric solution of dibucaine hydrochloride as an intrathecal injection toward the end of labor, was employed 13,299 times in this hospital during this six-year period. Due to a lack of 24-hour coverage by trained anesthetists in the birth room, saddle block anesthesia for delivery has been given by students and interns, under the supervision of residents, since 1946. Techniques were worked out to avoid the hazards of acute complications.

The records of 3,147 patients were reviewed. It was found that 25 were dead of causes not related to saddle block anesthesia. Two-thirds, or 1,998,

could not be located; 47 who were located were unable to return for examination. The department of neurology developed a preliminary neurological screening examination procedure, and this was given to the remaining 1,077 patients. They were

TABLE 1.—*Evidence of Patient Acceptance of Saddle Block Anesthesia*

	Saddle Block Anesthesia	
Subsequent Use, No.	Patients Accepting in Subsequent Births	Total
1	309	309
2	235	470
3	146	438
4+	59	236
Single	328	328
Total	1,077	1,781

questioned regarding dizziness on change of posture, unexplained headache, stumbling, and urinary incontinence. They were examined for muscle strength and coordination, by having them stand on the toes of both feet and then on each foot separately. They were also examined for paresthesias, abnormal reflexes, stretch reflexes (tendon), Babinski signs, changes in deep sensation, and relaxation of rectal sphincter.

Of the 1,077 patients who returned for examination, 981 were found to be free of all evidence of neurological abnormalities, either by history and/or neurological screening examination. There were 96 patients in whom some suggestive evidence of neurological abnormality was found. These patients were referred for complete neurological examination by members of the department of neurology. Sixty patients were thought to have altered reflexes on preliminary screening examination, but this was confirmed in only three by the neurological examination. The neurologist considered that the headaches and dizziness in only one of the 56 patients who complained of these symptoms was related to the saddle block anesthesia. The paresthesias in 2 of the 11 patients with suggestive sensory changes were thought to be due to the saddle block anesthesia, while in the other 9 patients it was due to other causes. Some patients had one or more of these signs and symptoms. Eleven of these 96 patients referred to the neurologist were unable to complete their neurological examinations for personal reasons.

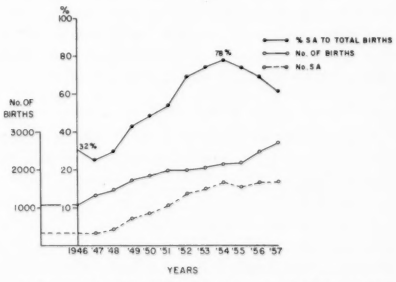
Only nine of the patients referred for neurological examination were found to show significant neurological deviations. An analysis showed that six of the nine had findings which were probably related to saddle block anesthesia. These consisted of absent or markedly decreased reflexes in three patients, sensory changes in the legs in two, and headaches and dizziness in one. In the other three patients, there was some question as to the relation of their symptomatology to saddle block anesthesia. Two of them had herniated disks, one in the thoracic region and one in the lumbar region. The third patient had severe headaches and dizziness for five years prior to, and continuing since, her first saddle block anesthesia. The neurologists were unable to find any neurological changes and felt that her headaches and dizziness were not caused by the anesthesia but may have been exaggerated by it.

Therefore, of the 1,077 patients examined, 9, or less than 1%, showed even suggestive changes on neurological examination which might be related to the saddle block anesthesia, and only 0.5% which were probably related to their anesthesia. This is an unusually low rate for late anesthetic complications of any kind. Our clinical experience does not indicate this method to be a hazardous form of anesthesia in obstetrics.

Comment

Though no case of serious complications resulted from saddle block anesthesia in our experience with 3,147 patients, the neurological screening examinations did reveal a rather large number of patients who had suggestive neurological complaints and signs of neurological changes. All but nine of these patients were cleared by the neurologist of deviations. In none of these patients had the symptoms been significant or incapacitating, and the 11 women who did not return for completion of the neurological examination refused because of their work schedule. The careful neurological examination identified only six patients with "probably related" and three patients with "possibly related" neurological deviations.

Since our study was made five or more years after the patients had received their first saddle block anesthesia, and as many of our patients are young women with recurrent pregnancies, many patients had had several saddle block anesthesias between the time of the termination of this study



Incidence of saddle block anesthesia in obstetrics at University of Arkansas School of Medicine, 1946-1957.

and the time of the examination. Some of the patients in the study group received as many as six subsequent saddle block anesthesias. The 1,077 patients examined in 1956 and 1957 had received 1,781 saddle block anesthesias at the time of the record review (table 1).

An analysis of the frequency of employment of saddle block anesthesia reveals that its use is increasing at our hospital. Forty per cent of the over 9,000 patients delivered in the years of this study (1946-1951) received saddle block anesthesia (70% of more than 13,000 from 1952 to 1957). It is noted that 31.7% of the patients delivered in 1946 at our hospital received saddle block anesthesia, while 78% of the patients in 1954 were given it (table 2 and figure).

TABLE 2.—*Incidence of Saddle Block Anesthesia in Obstetrics, 1946-1951, 1952-1957*

Yr.	Total Births	Saddle Block Anesthesia	
		No.	%
1946	1,065	338	31.7
1947	1,314	339	25.8
1948	1,481	440	29.6
1949	1,719	746	43.4
1950	1,840	893	48.5
1951	1,967	1,075	54.7
Sub totals	9,386	3,831	40.8
1952	1,964	1,584	69.5
1953	2,003	1,486	74.2
1954	2,169	1,680	77.9
1955	2,165	1,589	73.4
1956	2,459	1,646	68.2
1957	2,707	1,674	61.4
Sub totals	13,467	9,468	70.2

The greatly expanding use of intrathecal anesthesia for both obstetric and surgical procedures has established a large body of patients in whom unrelated neurological deviations might occur at a subsequent date. Makepeace,[5] in surveying the two series of late sequelae after saddle block anesthesia in 1949 and 1950 in St. Louis and Memphis, suggests that epidemic Coxsackie virus encephalitis might be responsible because of the geographical factor of the Mississippi Valley. In the interval after our study (1951-1957) several bizarre neurological manifestations have been noted at the University of Arkansas Medical Center, and these will be the subject of a subsequent report.

Conclusions

The records of 3,147 patients receiving saddle block anesthesia in 1946-1951 were analyzed, together with a careful long-term neurological follow-up of 1,077 patients. Six of the 1,077 patients exhibited neurological deviations which were probably related to saddle block anesthesia. These were minor, including alterations in reflexes, mild sensory changes in lower legs, headaches, and dizziness. No major neurological sequelae were found. Our experience would indicate that paralysis or severe complications from saddle block anesthesia are rare. This method of anesthesia given for delivery has proved to be clinically effective, safe, with a high degree of patient and physician acceptance. We believe that until better anesthesia is available, or until there is 24-hour coverage in the birth room by trained anesthetists, saddle block anesthesia is safer than inhalation anesthesia and more satisfactory for both patient and doctor than local anesthesia.

4301 W. Markham (Dr. Dodge).

The dibucaine used in this study was supplied as Nupercaine by Ciba Pharmaceutical Products, Inc., Summit, N. J.

Screening examinations were conducted by house officers of the Department of Obstetrics and Gynecology.

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CURRENT CONCEPTS OF THE MEDICAL MANAGEMENT OF ULCERATIVE COLITIS

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Ulcerative colitis, though presenting a difficult therapeutic problem, is capable of responding to prolonged and comprehensive medical management. The important therapeutic measures include rest, the use of sedatives and antispasmodics, nutritional and electrolyte repletion, transfusions of blood or plasma, injection of iron for iron-deficiency anemia, antibacterial medication, especially use of sulfonamides and skillful attention to the emotional problems. ACTH and various adrenal steroids are useful adjuncts to therapy, initiating and potentiating recovery, facilitating control of severe recurrences, and providing an opportunity for "total treatment." These compounds can be administered effectively for long periods with a relatively low incidence of serious complications.

While the cure of disease depends on knowledge of etiology and pathogenesis, numerous illnesses, including ulcerative colitis, may be managed effectively though their causes remain obscure. Ulcerative colitis continues to present a most formidable therapeutic problem. Nevertheless, advances in the management of nutritional and biochemical disturbances and in the treatment of infections, the use of corticotropin and the adrenal steroids, awareness of the contributory role of emotional disorders in the disease, and increased knowledge of the natural history of ulcerative colitis have improved the outlook significantly. The purpose of this paper is to review current concepts of the medical management of ulcerative colitis and to reemphasize their effectiveness.

The Nature of the Problem

Ulcerative colitis is an acute and chronic inflammatory and ulcerative disease of the colon and rectum.[1] The principal symptoms are rectal bleeding, diarrhea, abdominal discomfort, and cramping pain, fever, anorexia, and malnutrition. Proctoscopy usually demonstrates diffuse inflammation, congestion and edema of the mucosa, multiple tiny ulcerations, excessive bleeding, and bloody or purulent exudate. X-ray examinations reveal that the entire colon is affected in at least 50% of cases; varying segments of the intestine are diseased in 40%; and in 10% the process is relatively superficial and does not produce roentgenologically demonstrable changes. The adjacent terminal ileum is involved in perhaps 15 to 20% of patients. Ileocolitis affects chiefly the distal ileum, the cecum, and the ascending colon. Ulcerative colitis usually occurs among young people; most patients are below the age of 40 or 50 years, though no age is exempt. There is no sex predominance. A family history of ulcerative colitis is elicited in 5 to 10% of patients. Allergic disorders, such as hay fever, asthma, and drug sensitivity, are present in 20 to 30% of patients.[2] Other interesting associations are rheumatic fever, rheumatoid arthritis, and erythema nodosum.

The onset of the disease may be mild, with occasional rectal bleeding, or it may be severe, developing as an acute, febrile, toxic illness.[3] Fulminating ulcerative colitis is characterized by necrotizing inflammation of the intestine. The onset is abrupt, with high fever, toxemia, intense diarrhea, electrolyte depletion, dehydration, poor nutrition, and abdominal distention. In children the disease may begin very gradually; fever and anemia may be the principal symptoms and diarrhea may not be prominent initially. The circumstances at the onset of ulcerative colitis usually are obscure. The disease often occurs in previously healthy individuals; frequently it develops in chronological association with acute enteric or respiratory infections, pregnancy, or serious emotional difficulties.

Chronic ulcerative colitis is a disease with striking tendency to recurrence. Remissions are common in mild and moderate colitis but are relatively infrequent in the untreated severe disease. Recurrences are related to upper respiratory and viral infections, other intercurrent illness, operations, the use of antibiotics as in the treatment of respiratory infections, the menses, pregnancy, dietary indiscretions, physical fatigue, and emotional tension. Complications develop in the majority of patients, significantly influencing the course of the illness and the response to treatment. In the colon, the problems include giant ulceration, perforation, peritonitis, pericolitis, "toxic megacolon," hemorrhage, stricture, obstruction, pseudopolyps, polyps, carcinoma, perirectal abscess, fistula, electrolyte depletion, and defective absorption of food. The systemic complications include anemia, nutritional deficiencies, hypoproteinemia, hypergammaglobulinemia, rheumatoid arthritis, thrombophlebitis, uveitis and iritis, erythema nodosum, pyoderma gangrenosum,

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pyelonephritis, nephrolithiasis, fatty liver, hepatitis, cirrhosis of the liver, pancreatitis, adrenal depletion, osteoporosis, acute psychosis, hemolytic anemia, drug sensitivity, transfusion reactions, and amyloidosis. The number of complications in a single case may be considerable, as in a male patient who developed biliary cirrhosis, ascites, pancarditis, erythema nodosum, anemia, hypoproteinemia, steatorrhea, osteoporosis, acute arthritis, pyoderma, rectal fistula, and polyps. The mortality varies from 5 to 20% depending on the severity of the cases analyzed. Fatalities are more frequent during the first one or two years of illness, especially in patients with fulminating colitis. The more important causes of death are perforation of the intestine with peritonitis, hemorrhage, overwhelming infection, carcinoma of the colon, and surgical complications.

Despite considerable investigation, the cause of ulcerative colitis remains unknown.[4] Many causes have been postulated, including allergy to foods, nutritional and hormonal deficiencies, lymphatic obstruction, absence of "protective factors" in the intestinal wall, bacterial or viral infection, the destructive action of proteolytic enzymes or bacterial endotoxins, immunologic disorders including the Shwartzman and Arthus phenomena, antigen-antibody reactions and autosensitization of the colon, vasospastic, neurogenic, and psychogenic disturbances, abnormalities in the connective tissue of the intestinal wall, and metabolic disturbances. The irritable colon does not predispose to ulcerative colitis. Though amebic dysentery may rarely be followed by ulcerative colitis, parasitic infestations and bacillary dysentery do not predispose to the disease. Multiple causal factors probably are involved; on the basis of our clinical and laboratory observations an immunologic component, perhaps autosensitization of the colon, with or without the action of bacterial endotoxins, is a possibility; neurogenic stimulation of the intestine with vasospasm and secondary infection also appear important.

Objectives of Therapy.—The treatment of ulcerative colitis remains nonspecific, symptomatic, and comprehensive. Since the anatomic changes often are severe, and healing requires long periods of time, treatment must be prolonged. Certain therapeutic principles apply generally, but variations in the course of the disease necessitate adaptation of the program to the individual patient. The immediate objectives are physical and emotional rest, maintenance of nutrition, elimination of infection, restoration of normal intestinal function, and control of the associated emotional problems.[5] The ultimate goal, of course, is complete healing of the intestine and return of the patient to a normal life. The potentiality for reversibility in ulcerative colitis is considerable, perhaps greater than is appreciated, and this possibility provides the basis and the justification for continued medical management. The protracted illness, the many complications, and the frequent, expensive hospitalizations are understandably discouraging to the patient and his family. A lucid explanation of the illness and its treatment and a hopeful prognosis are helpful in securing the cooperation necessary for the prolonged therapy. Patience, perseverance, and equanimity are required of the physician undertaking the management of this difficult problem.

Rest, Sedative, and Antispasmodic Therapy

Physical fatigue and emotional tension contribute to the persistence and recurrence of ulcerative colitis. Rest and adequate relaxation diminish spasm and hyperactivity of the colon. Complete rest in bed in the hospital is indicated during the acute stage; hospitalization permits careful control of the patient and the environment and the establishment of an effective therapeutic program. In some cases hospitalization of three to six months or longer may be necessary to control the disease thoroughly. Adequate rest may be obtained through a combination of skillful nursing, long hours of sleep, and pleasant recreation. Sedatives, especially barbiturates such as phenobarbital (30 mg. four times daily), are helpful. Various tranquilizing drugs and appropriate dosages include hydroxyzine (Atarax) hydrochloride, 25-100 mg. four times daily; prochlorperazine (Compazine), 5-20 mg.; thiopropazate dihydrochloride (Dartal), 5-30 mg.; meprobamate (Equanil or Miltown), 4-800 mg.; promazine (Sparine) hydrochloride, 10-200 mg.; chlorpromazine (Thorazine) hydrochloride, 10-200 mg.; perphenazine (Trilafon), 2-16 mg.; and phenaglycodol (Ultran), 3-600 mg. Chloral hydrate, 1 Gm., secobarbital (Seconal), 100 mg., pentobarbital (Nembutal), 100 mg., Tuinal, a combination of equal proportions of sodium seconal and sodium amytal, 100 mg., and glutethimide (Doriden), 0.5 Gm., are among many compounds which can be prescribed at bedtime to facilitate sleep.

Antispasmodics tend to reduce spasm and hypermotility of the intestine, though their effects are extremely variable. Tincture of belladonna, 10 drops four times daily, and atropine sulfate taken orally, 0.005 Gm. several times daily, have long been prescribed for this purpose. Many other effective antispasmodic, anticholinergic drugs are available; including diphemanil (Prantal) methylsulfate, 100 to 200 mg. four times daily; piperphenamine (Darstine), 100 mg.; penthienate bromide (Mondronal), 5 mg.; propantheline (Pro-banthine) bromide, 15 to 30 mg.; oxyphenonium bromide (Antrenyl), 10 mg.; methscopolamine (Pamine), 2.5 mg.; tridehexethylchloride (Pathilon) chloride, 50 to 100 mg.; and hexocyclium methyl sulfate (Tral), 25 mg.

To suppress the hyperactive gastrocolic reflex, these drugs are prescribed more effectively before meals and at bedtime. The individual response and the clinical tolerance for anticholinergic compounds varies considerably, necessitating selection of the

drug most useful in each case. In severely ill, malnourished patients and in children, the potent antispasmodics may suppress intestinal motility so completely as to produce atony. The abdominal distention and absence of audible peristaltic activity, together with the fever, may suggest peritonitis; however, intestinal motility usually returns within 48 to 72 hours after the medication is discontinued.

Severe abdominal cramping pain and rectal tenesmus temporarily may require the use of deodorized opium tincture (10 drops three or four times daily), codeine sulfate (0.03 Gm. four times daily), morphine sulfate (0.015 Gm.), or meperidine (50 to 100 mg.). Opiates are not prescribed routinely or for long periods, to avoid the possibility of addiction; opiates, by increasing intestinal spasm, occasionally intensify rather than lessen the abdominal discomfort. Heat applied to the abdomen by means of an electric pad or hot water bottle also relieves the abdominal discomfort. The prolonged diarrhea of ulcerative colitis may cause anal irritation; compresses of witch hazel, hot sitz baths, and local anesthetic ointments will relieve the discomfort and facilitate healing.

Management of Emotional Problems

Ulcerative colitis does not appear to be primarily of psychogenic origin, but emotional disturbances are demonstrable in the majority of cases, if not in all. The patients are described psychiatrically as dependent, immature, self-depreciating, obsessive-compulsive, hostile individuals, highly vulnerable to the ordinary events of life, perhaps because of feelings of humiliation, loneliness, helplessness, and hopelessness.[6] The psychiatric problems occasionally involve severe depression, schizophrenic and paranoid reactions, and suicidal attempts. The specificity of the emotional difficulties and their importance in the pathogenesis of ulcerative colitis require further elucidation. The psychogenic factors may reflect an important predisposition to the disease, or they may represent the secondary emotional manifestations of prolonged physical illness, disappearing when the disease is controlled or cured. Nevertheless, the emotional difficulties influence the course of the disease and the therapeutic response adversely. Thorough knowledge of the patient's emotional problems and skillful management of them are indispensable to the effective treatment of ulcerative colitis. On the other hand, the resultant symptomatic improvement does not necessarily establish the causal importance of the psychogenic factors.

Formal psychotherapy is indicated for the seriously disturbed patient. Though its permanent value has not been established conclusively, the approach often is helpful, especially in cooperation with the internist. Caution is necessary during the acute stage of ulcerative colitis, for the patient then is unable physically and emotionally to deal effectively with his problems; the resulting conflicts may aggravate the colitis and precipitate serious complications. Emphasis exclusively on the psychiatric aspects is unwise because of the hazard of inadequately treated or unrecognized organic disease; a case in point is that of a young man who previously had undergone operations for regional enteritis and intestinal obstruction. Persistent severe pain in the rectum had been attributed to an emotional disturbance and psychotherapy had been maintained for several months, though the patient had not been examined. Rectal examination easily demonstrated a large ulceration of the rectum with severe inflammation and muscle spasm; the pain subsided when the ulcer healed. Neglect of the psychiatric difficulties also is likely to retard the response of the patient. In general, the most helpful psychotherapy is administered by the well-informed, interested, and sympathetic attending physician, constantly providing reassurance and encouragement. The patient-physician discussions may disclose a difficult or frustrating problem at work or at home, readily dealt with on a commonsense basis, resolution of which may improve the course of the disease decisively. The objective of this approach is protective, ego-strengthening reorientation rather than fundamental reorganization of the patient's personality. Sustained physical and psychogenic improvement is reflected in the development of confidence, poise, and a more mature approach to life. Frequently, and especially in children, psychotherapy also must be directed to the parents. Indeed, the success of therapy may be determined by the ability to influence the family environment to the benefit of the patient. Psychoanalysis, in a small group of patients, apparently has not produced significant permanent benefit. The value of electric shock therapy[7] and lobotomy in patients with ulcerative colitis remains to be established.

Diet, Nutritional Considerations, Electrolytes, and Fluids

Ulcerative colitis is not caused by nutritional deficiencies, food allergy, or roughage in food. However, a diet without the mechanical and chemical irritants contained in fruits, vegetables, fruit juices, condiments, alcoholic beverages, and excessively hot or cold foods decreases the abdominal distress and the diarrhea. A more limited menu, consisting of farina, cream of wheat, toast, butter, soft boiled eggs, clear broth, tea, boiled rice, jello, and custard may be utilized temporarily in the acutely ill patient. A bland diet with meat and potatoes but without fruits and vegetables usually is prescribed initially. Cooked or canned fruits and vegetables are added when the feces are consistently well formed and do not contain occult blood. The diet is liberalized as the improvement continues. For psychological reasons dietary restrictions are less rigid for children with ulcerative colitis; indeed, the bland diet should not be permitted to

assume overwhelming significance for any patient, as conflicts between the limitation of food and the psychogenic disturbances resulting therefrom should be resolved in favor of the emotional considerations. The clinical improvements associated with the avoidance of fruits, bran cereals, and milk seem attributable most likely to the elimination of high-residue foods; milk especially may increase the flatulence, abdominal discomfort, and diarrhea.

Nutritional deficiencies are very common in ulcerative colitis, as a result of the reduced intake of food, the increased tissue catabolism, loss of blood, and the tremendous loss of nitrogen in the feces. The importance of restoring normal nutrition in patients with ulcerative colitis hardly can be overemphasized; in some cases this alone may suffice to initiate significant improvement. The diet, therefore, should provide adequate amounts of proteins and calories, perhaps 2,500 to 3,500 calories including 125 to 150 Gm. of protein daily. Supplements may be added, though good-quality whole foods are preferred. Protein anabolic agents, such as testosterone propionate and norethandrolone (Nilevar), may be prescribed to increase the retention of nitrogen in the tissue. The cooperation of a competent and interested dietitian is invaluable in providing appetizing menus and in encouraging the patient to eat sufficient quantities of food. Complete nutritional restoration requires at least three months and often longer. Rapid transit of food through the hyperactive intestinal tract and concomitant disease of the ileum may interfere with normal absorption, resulting in steatorrhea. The presence or absence of malabsorption is indicated by measurements of the plasma carotene and fat excretion in the feces. In the presence of steatorrhea, the fat intake may be limited to 75 or 50 Gm. daily; adrenal steroids are useful in the management of this problem. Tube feeding with protein supplements or liquefied homogenized foods, and concomitant constant suction of the distal small intestine, may be helpful in selected cases, but this procedure rarely has been necessary in my experience.

The severe diarrhea of ulcerative colitis causes excessive losses of potassium, sodium, and chloride from the intestinal contents and dehydration. Solutions of 5% dextrose in isotonic sodium chloride solution, containing appropriate quantities of potassium salts, are necessary to correct the electrolyte and fluid deficiencies. Fluids may be administered for long periods via a polyethylene catheter introduced into a small vein; however, this procedure is potentially hazardous because of the possibility of secondary infection, especially in patients receiving steroids, and it is not recommended in patients receiving both antibiotics and steroids. Measurements of the fluid intake, urine output, and of the serum electrolytes provide useful information. Complete reliance on these indexes probably is unwise, for the serum sodium and potassium may be normal, at least temporarily, in the presence of depletion of electrolytes. The excessive loss of calcium in occasional patients with steatorrhea necessitates the intravenous administration of calcium salts.

Transfusions of whole blood, 500 to 1,000 ml., are indicated for moderate or severe hemorrhage and for anemia and hypoproteinemia; the amounts required may be estimated from the hemoglobin, erythrocyte count, hematocrit, and, if available, the blood volume. The frequency of transfusion reactions in the colitis patient necessitates the most careful blood typing and cross matching; the blood should preferably be administered slowly at room temperature. Addition of an antihistaminic may reduce the incidence of reactions. Plasma, 500 to 1,000 ml., stored at room temperature, and human albumin, 50 Gm. injected intravenously, are useful in correcting hypoproteinemia when the food intake is low. Protein hydrolysates probably are less satisfactory for this purpose because of rapid metabolism, but they may be administered. The newer intravenously given fat emulsions provide an additional source of food and calories; substantial amounts may be administered without apparent untoward effects. Iron-deficiency anemia is very common as a result of the reduced intake of food and the chronic loss of blood from the intestine. In the absence of profuse rectal bleeding, anemia may be corrected by intramuscular administration of an iron-dextran complex (Imferon), 1.0 to 2.0 Gm., in divided doses; the hematological response is evident within several weeks. Iron administered orally is often irritating to the gastrointestinal tract in patients with ulcerative colitis, though several newer preparations are alleged to be less troublesome in this respect and ferrous sulfate taken orally with meals may be tolerated by some patients. Multivitamins are useful nutritional adjuncts; B complex preparations may be added to the intravenously given fluids or injected intramuscularly. Excessive quantities of vitamins are unnecessary; preparations such as ascorbic acid are irritating to the intestine when taken by mouth. Severe bleeding in ulcerative colitis usually originates in the highly vascular intestinal wall. Occasionally in patients with associated hepatic disease or with defective intestinal absorption the prothrombin time may be prolonged, contributing to the bleeding, but the parenteral administration of vitamin K will correct the abnormality.

Sulfonamides and Antibiotics

Although a bacterial or viral causative factor has not been established, the fever, the inflammation demonstrable proctoscopically and histologically, and the toxemia and complications such as perirectal abscess and pericolitis suggest an intestinal infection. There is no consistent correlation between the identifiable bacterial flora of the intestine and the clinical course of ulcerative colitis, although occasionally the subsidence of symptoms coincides with the disappearance of hemolytic col-

iforms, staphylococci, and streptococci from the feces. Sulfonamides may be prescribed in ulcerative colitis to control or prevent secondary infection and in the hope of eliminating unidentified bacterial causes of the disease. Sulfonamides may also be administered during the use of ACTH and the adrenal steroids to prevent secondary infection. The total bacterial count in the feces will decrease as a result of eliminating the coliform organisms, and the fecal flora will change from gram-positive to predominantly gram-negative. The long-term effects of prolonged sulfonamide therapy on the bacterial flora of the feces have not been studied thoroughly.

No single sulfonamide excels all others, in my experience, although several appear to be especially useful. These include sulfaguanidine, 8 Gm. daily; salicylazosulfapyridine (Azulfidine), 4 to 8 Gm.; phthalylsulfathiazole (Sulfathalidine), 4 to 6 Gm.; succinylsulfathiazole (Sulfasuxidine), 8 to 12 Gm. daily; sulfadiazine and sulfisoxazole (Gantrisin) 4 to 6 Gm. daily. The sulfonamides usually should be administered continuously rather than intermittently. Soluble compounds, such as sulfadiazine, may be given as retention enemas in doses of 1 or 2 Gm. in 30 or 60 ml. of water or isotonic sodium chloride solution; beneficial results are noted in patients with relatively localized colitis. Para-nitrosulfathiazole (Nisulfazole) may be administered rectally as a 10% suspension in quantities of 1 or 2 oz. (28 or 57 Gm.). The beneficial clinical effects during sulfonamide therapy are observed initially in numerous cases and may continue for weeks, months, or years. More often, however, the response gradually decreases, presumably because either the original flora are restored or resistant bacteria develop. A change in sulfonamide may renew the clinical response; sulfonamide drugs thus may be alternated effectively for long periods. Sulfonamides may cause adverse side-effects, including fever, nausea, vomiting, flatulence, and headache, and dermatological, hematological, and renal complications, although their incidence is relatively low. The temporary antibacterial effects, the development of bacterial resistance, and the variable clinical responses are important limitations. Nevertheless, the sulfonamides seem to be helpful adjuncts, probably contributing to the control of the disease and decreasing, though not eliminating, the hazard of serious infection.

Penicillin (1 to 2 million units daily) and streptomycin (1 to 2 Gm. daily) may be administered intramuscularly together for the same reason as the sulfonamides. They seem indicated during the acute febrile stage of the illness and in the management of pericolitis when medication by mouth is discontinued temporarily. The antibacterial effects of chlortetracycline (Aureomycin), chloramphenicol (Chloromycetin), oxytetracycline (Terramycin), tetracycline (Achromycin), and neomycin sulfate resemble those of the sulfonamide drugs: tetracycline and neomycin sulfate perhaps are the most effective of this group. The clinical response occasionally may be favorable, but since these compounds cause disturbing gastrointestinal side-effects, including glossitis, stomatitis, nausea, flatulence, diarrhea, perianal itching, and a proctitis, not unlike ulcerative colitis, they are not prescribed routinely. An exception to this principle is the very occasional use of tetracycline (1 Gm. by mouth daily) for pyoderma. The use of antibiotics, including penicillin administered orally, in the treatment of respiratory infections among colitis patients should be avoided because of the possibility of aggravating or reactivating the disease.

Corticotropin (ACTH) and Adrenal Steroid Therapy

The use of corticotropin (ACTH) and the adrenal steroids in ulcerative colitis is based on several considerations, among them the limitations of conventional treatment, the chronicity and progression of severe colitis, and the numerous complications, including rheumatoid arthritis, erythema nodosum, myocarditis, and iritis, responsive to corticoid therapy. ACTH and the adrenal steroids do not cure ulcerative colitis, prevent recurrences completely, or replace established methods of treatment, but they are useful, at times dramatic, adjuncts when administered in sufficient quantities for adequate periods of time and under carefully supervised conditions.[2] The improvement produced is similar to that observed in the absence of steroids but it is more frequent, more rapid, and more complete. The response is characterized by the prompt disappearance of fever, toxemia, abdominal discomfort, and diarrhea; by increased appetite and by a remarkable sensation of well-being. While the psychological benefits are not inconsequential, the steroid effect involves demonstrable healing, as noted in histological studies of rectal biopsies. The proctoscopic changes subside gradually; the rectal mucosa eventually may appear normal or slightly granular and hyperemic. Laboratory indications of the favorable response include the lowering of elevated sedimentation rates and the return of serum mucoprotein levels to normal, disappearance of blood from the feces, subsidence of the nitrogen loss in the feces, and restoration of the normal pattern of plasma proteins. Rectal biopsies demonstrate histologically the disappearance of edema, cellular infiltration, and ulceration, reconstitution of the normal ground substance of the connective tissue of the intestine, and restoration of the basement membranes of the epithelium of the colon.

The quantities of ACTH and the adrenal steroids required in ulcerative colitis exceed the amounts effective in other diseases; relatively large quantities for long periods are necessary to control the disease completely. Aqueous corticotropin, the most potent compound, should be administered intramuscularly in doses of 30 mg. every six hours, 120 mg. per day; 160 or 200 mg. daily may be given

temporarily in selected cases. ACTH administered intravenously, in quantities of 10 or 20 U. S. P. units contained in 500 cc. of 5% solution of dextrose in distilled water, every 12 hours, is the most potent stimulant of adrenocortical function. Corticotropin gel or corticotropin-zinc hydroxide has been prescribed chiefly as maintenance therapy in single daily doses of 40 or 80 mg. The orally administered steroids in decreasing order of effectiveness in ulcerative colitis are hydrocortisone (200 mg. per day initially), prednisone or prednisolone (60 to 80 mg.), and cortisone (300 mg.). Hydrocortisone also may be given intravenously in quantities of 50 mg. every 12 hours, and intramuscularly in doses of 50 to 100 mg. every 4 or 6 hours. Steroids administered as retention enemas once or twice daily or by continuous drip appear to be helpful in some patients; the advantages of this procedure presumably are maximal concentration of the steroid in the diseased area and a lesser tendency to side-effects,[8] however, systemic steroid effects may occur when sufficiently large amounts of steroids are administered intrarectally. The preparations administered by this route include hydrocortisone sodium succinate (100 or 200 mg. in 15 to 250 ml. of water or isotonic sodium chloride solution) and prednisone (15 to 30 mg.) together with phthalylsulfacetamide and the newer steroid, methylprednisolone (Medrol, 60 to 80 mg. in 15 to 30 ml. of water). Clinical and proctoscopic improvements have been observed within 7 or 10 days. Opiates, including tincture of deodorized opium, codeine, or morphine, may be required to facilitate retention of the steroid solution. Hydrocortisone also has been prepared in the form of rectal suppositories, each containing 10 to 15 mg. and prescribed three or four times daily; the value of this type of medication is not yet established. Several new oral compounds, triamcinolone (Aristocort, Kenacort, 20 to 30 mg. daily) and methylprednisolone (20 to 32 mg. daily) are helpful occasionally. On the basis of present evidence, the effects of the new steroids do not appear to excel those of hydrocortisone or prednisone in ulcerative colitis. As with other medication, the response varies considerably among individuals and in the same patient at different times, necessitating identification of the steroid and the maintenance dose most effective for a given individual, as in the patient not responding to large doses of prednisone, or hydrocortisone, in whom symptoms subsided when given methylprednisolone.

The steroids are continued usually for several months and in many instances for years, as a practical means of maintaining patients in satisfactory health without surgery. The initial doses are decreased gradually, depending on the individual course. When the daily intake of ACTH reaches 40 to 60 units this compound may be replaced by hydrocortisone, prednisone, or one of the newer hormones. The transition is accomplished by arbitrarily exchanging 1 mg. of prednisone or 2 mg. of hydrocortisone for 1 unit of ACTH. Effective minimal or maintenance doses then are determined for each patient; these usually are for ACTH, 20 to 40 units daily; for hydrocortisone, 40 to 80 mg.; for prednisone, 15 to 30 mg.; for methylprednisolone, 12 to 20 mg.; and for triamcinolone, 12 to 20 mg. Periodic adrenocortical stimulation with corticotropin, though theoretically rational, has not appeared necessary. Recurrences during steroid therapy usually are related to respiratory infections, fatigue, tension, and especially to premature reductions in dosage. Occasionally, the therapeutic effect diminishes after the prolonged or intermittent administration of steroids. The mechanism of the waning response is not known; it may be related to increasing severity of the disease, the development of circulating antihormones, or partial inactivation of ACTH by tissue enzymes at the site of injection. However, a similar clinical tolerance may develop with the orally administered compounds. The response may be restored by increasing the quantity of medicament, by changing the compound, or by the readministration of corticotropin. In a patient 59 years of age the response to ACTH was excellent initially but nil during a subsequent recurrence; a similar trend was observed later with prednisone and with hydrocortisone. Currently, symptoms seem to be responding to triamcinolone but the outlook is uncertain, perhaps because of unresolved serious emotional problems. In 10 to 15% of patients with ulcerative colitis, steroids fail to influence the disease even temporarily; the factors involved are not known, though emotional disturbances seem to be important. In a small number of patients drug sensitivity or allergy to ACTH limits the use of this preparation.

ACTH and the adrenal steroids should not be prescribed routinely in ulcerative colitis, for numerous patients respond satisfactorily to symptomatic supportive therapy without the adrenal hormones. The principal indications are severe disease, recurrent despite thorough medical management in the hospital; acute fulminating colitis; and the presence of arthritis, iritis, and erythema nodosum. Steroids are contraindicated in the presence of perforation of the intestine, peritonitis, and abscess formation. In severe ulcerative colitis complicated by malnutrition, electrolyte imbalance, and overdistention of the colon, steroids should be prescribed with the utmost caution during the rapid correction of these conditions. Steroids are not contraindicated necessarily in the presence of hemorrhage or pericolitis with peritoneal irritation, for these complications may respond dramatically. Pseudopolypoid formation is not a contraindication, for a sustained favorable response to steroids may decrease the tissue hyperplasia significantly. A history of diabetes mellitus or tuberculosis does not exclude the use of hormones, provided the indications otherwise are acceptable and appropriate supportive therapy is prescribed. Peptic ulcer is not an abso-

lute contraindication, for the incidence of ulcer during the steroid treatment of ulcerative colitis is low and colitis patients with a history of ulcer may take the hormones without apparent harmful effects.

Steroid therapy, in most cases, must be maintained for long periods, as premature reduction in dosage or discontinuation of medication is not infrequently followed by the relapse or recurrence of symptoms. Ideally, the steroids are discontinued when the feces contain no occult blood, bowel function is normal, the blood cell counts and sedimentation rates have returned to normal, and there is proctoscopic indication of healing. Roentgenologic evidence of healing, except for the disappearance of marginal serration and ulceration, is not to be expected in ulcerative colitis until after prolonged improvement. While the withdrawal of steroids may occasionally be difficult, the gradual discontinuation of medication in patients who have responded adequately usually is accomplished uneventfully.

ACTH and the adrenal steroids are capable of causing many complications.[9] The most common are the symptoms of adrenal cortical hyperfunction, or Cushing's syndrome (edema, moon-face, acne, "buffalo obesity," and hypokalemic hypochloremic alkalosis). Hypertension, hyperglycemia, glycosuria, and various infections, not uncommon with ACTH and cortisone, are less frequent with the newer compounds. Restriction of sodium chloride has been less necessary with the newer steroids. Emotional disturbances, including psychotic reactions, occur in 15% of cases and constitute an important but reversible complication. The development of steroid psychosis necessitates prompt discontinuation of the medication and sedation; chlorpromazine, 100 or 200 mg. daily, is especially valuable for this purpose. The striking improvement in the colitis during the psychosis is of interest.

Giant ulceration, perforation of the intestine, and hemorrhage, important complications of the disease in the absence of steroids, have not increased in frequency during hormonal therapy, in my experience. Persistent hemorrhage in ulcerative colitis usually is ascribable to the intense vascularity of the hyperplastic intestinal wall, and steroids occasionally reduce the bleeding by decreasing the tissue hyperplasia and perhaps by decreasing vascular permeability. Excessive friability of the intestinal wall has not been encountered in those patients given steroids and later requiring operation. The incidence and severity of complications during steroid therapy can be reduced by constant, careful clinical and laboratory observations, by the routine prophylactic administration of sulfonamides, and by the prompt correction of anemia, hypoproteinemia, and electrolyte and fluid imbalance. Frequent measurements of the serum electrolytes, erythrocyte and leukocyte counts, blood sugar level, and urine facilitate early recognition and prompt treatment of the various complications. Potassium deficits are corrected by the intravenous administration of 40 to 160 mEq. of potassium chloride daily; orally administered potassium salts are irritating to the intestine in many patients with ulcerative colitis and are not prescribed routinely.

In general, the adrenocortical hormones appear to be useful adjuncts to the comprehensive treatment of ulcerative colitis, acting as "therapeutic bridges," initiating and potentiating the recovery phase, facilitating control of severe recurrences, and providing an opportunity for "total treatment." Their use at present seems to have lowered the mortality and to have decreased the need for surgery. When prescribed with proper supervision and vigilance, the adrenal steroids can be administered with relative safety for long periods to patients with ulcerative colitis. Under steroid therapy rectal strictures decrease or disappear, and the roentgenologic appearance of the colon may improve significantly. Not infrequently, the clinical response is maintained for years after discontinuance of the steroid therapy.

The precise mechanism of action of ACTH and the adrenal steroids is not known. There is no evidence of direct pituitary or adrenal dysfunction in ulcerative colitis and the fundamental character of the disease apparently is not altered permanently by corticoid therapy. As in other illnesses, the steroids reduce the vascular and tissue responses to inflammation and suppress the accompanying toxic reaction. Perhaps they also influence some type of hypersensitivity mechanism in ulcerative colitis or inhibit the production of bacterial endotoxin within the colon. Their ultimate effect on the course of the disease and on the fundamental disease process remains to be determined.

Miscellaneous Materials

Many drugs and techniques have proved ineffective in the treatment of ulcerative colitis. These include antilysozyme compounds, polyvalent antidysentery serum, bacteriophage, antihistaminics, antithyroid drugs, ascorbic acid, cobra venom, enemas containing chemicals such as chloroazodin (Azochloramid), tannic acid, acriflavine, and silver nitrate, parathyroid extract, intracolonic administration of oxygen, hydrochloric acid, insulin, isoniazid, liver extract, epinephrine, posterior pituitary injection (Pituitrin), mucin, rutin, and salicylates. Enemas containing cod liver oil or aluminum hydroxide and kaolin may provide symptomatic relief in mild colitis but they do not influence the disease significantly. Psyllium hydrophilic mucilloid (Metamucil), by absorbing excessive fluid from the feces, may produce a more formed bowel movement. The combination powder of bismuth subcarbonate, calcium carbonate, and calcium phosphate, in equal doses of 1.3 Gm. each, is prescribed occasionally for a similar purpose. Elimination diets have not proved especially helpful, in my experience. The

clinical effect of various vaccines probably is analogous to the "non-specific protein shock" produced by typhoid vaccine, artificial fever, or foreign protein. There appears to be no satisfactory rationale for the administration of acid-alcohol extracts of intestinal mucosa from hogs in ulcerative colitis. The use of antiamebic drugs for presumptive amebic infections is ineffective in ulcerative colitis and often increases the abdominal discomfort and the diarrhea.

Surgical Considerations

The frequent recurrences of the disease and the recent improvements in surgical technique have increased interest in the operative treatment of ulcerative colitis.[10] In my experience, surgery is required in 10 to 15% of patients. The absolute indications are perforation of the colon, extensive polyposis, carcinoma, persistent massive hemorrhage, and stricture of the colon with obstruction. Colectomy may be necessary in patients with extensive persistent perirectal infection and fistula formation. Surgery also may be required in patients not responding to comprehensive medical management, including steroids, in the hospital. "Chronic invalidism" and "failure of medical treatment" are highly arbitrary designations, requiring thorough evaluation. Careful analysis often reveals inadequate treatment rather than irreversible disease. Thus, many patients previously advised to undergo surgery have responded satisfactorily to skillful medical management. An outstanding example is that of a young woman with severe colitis, who, in 1934, was advised to undergo an ileostomy. The procedure was delayed by an upper respiratory infection, and during this interval the clinical improvement was so pronounced that operation was postponed indefinitely. The proctoscopic appearance of the intestine gradually returned to normal. Subsequently, there was striking reversibility in the roentgenologic appearance of the colon. The patient remains well nearly 25 years later, without surgical treatment. Similar reversibility of the disease has been noted recently in two patients, one of whom was advised to undergo surgery in 1946 and in both of whom the roentgenologic appearance of the colon now is normal. The decision for operation should not result from frustration with a difficult problem nor should it be determined exclusively by economic considerations, though the financial burden imposed by the illness cannot be ignored.

The increased incidence of carcinoma in patients with ulcerative colitis presents a serious therapeutic dilemma.[11] Surgery often is advised in patients with colitis of 10 or more years' duration, as a preventive measure. However, routine colectomy and ileostomy in young men and women, otherwise in excellent health, seems undesirably radical; careful evaluation of each patient clinically, roentgenologically, and by exfoliative cytological study of colonic washings seems preferable. There is no decisive evidence that inflammatory pseudopolyposis directly predisposes to carcinoma in ulcerative colitis; hence, this situation is not necessarily an indication for operation. Surgery is not indicated for rheumatoid arthritis, anemia, iritis, or pyoderma gangrenosum, except under unusual circumstances, since these complications respond to medical management. Patients with cirrhosis, portal hypertension, and esophageal varices with hemorrhage may undergo portacaval or splenorenal shunts successfully and subsequently maintain satisfactory health without need for colectomy. Surgery is hazardous and usually contraindicated in patients with ileocolitis; the associated steatorrhea may be identified by measurements of the plasma carotene and the excretion of fat in the feces.

When surgery is necessary in ulcerative colitis, the procedure of choice usually is total colectomy and ileostomy performed in one or two stages. Chemotherapy and advances in medical and surgical care, in anesthesia, and in operative technique have reduced the operative mortality significantly. Improvements in the construction of the ileostomy [7] and in ileostomy appliances, and intelligent discussion of the operation with the patient, together with the helpful advice of other ileostomy patients, have greatly facilitated the adjustment to the procedure.

Ileostomy alone does not cure ulcerative colitis. Subtotal resection of the colon and anastomosis of the ileum to the sigmoid or rectum seems possible only in those few patients who are without demonstrable involvement of the rectum. Abdominoperineal resection is necessary when the rectum is severely diseased and the source of recurrent bleeding and infection. In segmental colitis of the cecum, ascending colon, or transverse colon which does not respond to adequate medical treatment, the operative procedure usually is limited resection and restoration of normal intestinal continuity. The procedures of vagotomy and pelvic autonomic neurectomy apparently have not been adopted generally. A unique surgical approach involves electrocoagulation of a small prefrontal area in the brain, attempting to interrupt the connection between the frontal convolutions, the thalamus, and the hypothalamus. The objective presumably is to eliminate cerebral control of the autonomic centers in the diencephalon and to decrease neurogenic stimulation of the intestine; the rationale and the effectiveness of this procedure in ulcerative colitis cannot be evaluated at present.

Surgical treatment often is the only effective method of restoring patients with chronic ulcerative colitis to a useful life; at times, the operation is lifesaving. However, the operative results are not uniformly successful.[12] The possible complications after surgery include bleeding, prolapse, infection, fistula formation, perforation and stenosis of the ileostomy, ulceration of the skin, intestinal obstruction, the development of enteritis, and severe electrolyte and

fluid deficiencies. The inadequate intake of food, excessive loss of nitrogen in the feces, and the prolonged administration of large amounts of steroids may cause serious nutritional depletion, delaying wound healing and predisposing to infection. However, the careful use of steroids and prophylactic chemotherapy and adequate nutritional care permit many patients to negotiate the surgical procedure without serious difficulty. In such cases the quantity of steroids is increased temporarily, immediately preceding, during, and after operation (cortisone, 300 mg., or hydrocortisone, 200 mg. intramuscularly or 100 mg. intravenously for 24 hours). The medication can be discontinued gradually during the first two weeks of convalescence, if so desired.

Comment

The chronicity, recurrences, and many complications of ulcerative colitis present a uniquely complex therapeutic problem. Treatment continually is dominated by the critical question as to the potential reversibility of the disease; the answer, not easily given, will determine the choice between medical or surgical management. If the patient responds favorably to medical treatment, will the effect be sustained? Is colitis ever cured or can it be controlled sufficiently to permit an economically self-sufficient, useful life? What constitutes "medical failure"? What are the dangers of chronic invalidism for the adult, retarded growth development for the child, or life-threatening complications for all patients? These problems are less critical in those with mild or moderately severe ulcerative colitis. Individuals with mild, remitting disease respond to conventional therapy with rest, sedation, antispasmodics, diet, vitamins, antibacterial therapy, and the "psychotherapy" provided by the attending physician. Patients with moderate or severe colitis, in addition, may require transfusions of blood and plasma, parenterally given fluids, iron given intramuscularly, and ACTH and the adrenal steroids. Although the disease tends to recur, the response to these treatments often is favorable.

The therapeutic problem is most critical, of course, in patients with fulminating colitis, continuously active colitis, or severe recurrent disease. The differing opinions concerning medical therapy and surgical treatment concern these cases particularly. In this dilemma, the advances in surgical technique seem to offer a most attractive and apparently rational solution. Complete removal of the colon and rectum does indeed "cure" the disease, with highly satisfactory, occasionally dramatic results. Nevertheless, as emphasized previously, surgery does not always solve the problem of the colitis patient; and ileostomy, no matter how effective, is not the ideal solution. The course after operation may be more serious than previously, as in a young man who died from diarrhea with extreme electrolyte depletion and dehydration, a young man who developed recurrent obstruction of the ileostomy and extensive enteritis, terminating in death, or the young woman who, after total colectomy and ileostomy, developed obstruction of the ileostomy, ascending ileitis, volvulus of the small intestine, subdiaphragmatic abscess, an abdominal pseudocyst, iron-deficiency anemia, recurrent intestinal obstruction, perforation of the small intestine, and fatal peritonitis. The vast majority of experienced physicians and surgeons accept the fact that most patients with ulcerative colitis, perhaps 80 to 90%, are capable of responding to thorough medical management, especially if the program emphasizes complete healing of the active disease during prolonged hospitalization, maintenance of general health, identification and resolution of emotional problems, avoidance of dietary or medicinal agents known to precipitate recurrences or aggravate the disease, added precautions during respiratory infections and other intercurrent illness, and avoidance of fatigue, loss of sleep, overwork, and excessive responsibility.

The therapeutic problem, then, is to select the 10 to 15% of patients with irreversible disease or with complications unresponsive to medical measures. This selection should not be arbitrary, for it often is difficult to predict initially the degree of improvement to be anticipated in many patients. Some individuals with apparently hopeless colitis improve dramatically on medical treatment and remain well. Other patients appearing less severely ill initially for some unknown reason fail to respond and ultimately require surgery. Therefore, except in the presence of serious complications, it has seemed more desirable to undertake detailed observation and a "therapeutic test" under careful supervision in the hospital. Patience and unremitting care are indispensable ingredients to the successful medical management of ulcerative colitis. The emphasis should be on total treatment, with utilization of all appropriate measures. The many favorable responses to prolonged medical management and the occasional transitions of diseased intestine to normal emphasize the potential reversibility of ulcerative colitis.[13] A significant corollary of this concept is the expectation that the knowledge from additional clinical studies of the disease, together with laboratory investigations of the problem, eventually will produce more effective treatment of this devastating illness.

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CONGENITAL BRANCHIOGENOUS ANOMALIES

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and
Col. Robert S. Higdon (MC), U. S. Army

Branchiogenous anomalies are of interest because of the varying clinical pictures they present after secondary infection or occlusion. Although the diagnosis of a branchiogenous anomaly may be evident, at times, it is difficult to evaluate the depth or extent of the associated tract. The differential diagnosis includes tuberculous and nontuberculous lymphadenitis, other infectious processes, tumors of the carotid, hygroma, dermoid cysts, lipomas, neurofibromas, hemangiomas, and lymphangiomas. Thorough surgical evaluation and competent extirpation should be carried out. Inadequate treatment of these lesions by sclerosing agents, such as phenol, or by incomplete electrosurgical measures often results in partial obliteration of these tracts, with subsequent secondary infection and unnecessary scarring and disfigurement.

Persons with congenital anomalies of branchiogenous origin present varied and interesting clinical findings. Occurring about the ears or on the neck, these lesions may appear in some patients only as insignificant, asymptomatic pits and in others as evident cysts or fistulas. Such lesions may be unilateral or bilateral, and they may be associated with other congenital anomalies. In some cases, because of the depth or the partial or complete obstruction of their tracts, or because of secondary infection, they may offer problems in diagnosis and therapy. This paper is a summary of the cases of 21 hospitalized patients with branchiogenous anomalies seen at Walter Reed Army Medical Center from 1950 to 1955.

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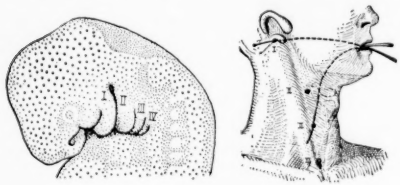
Classification and Development

Classification and Nomenclature.—Various classifications and nomenclatures for lesions of branchiogenous origin have been offered. The two broad



A *B*

Fig. 1.—A, human stages of branchial arches at 5 weeks. *B*, anomalies of branchial apparatus in man showing relationships of cysts and fistulas (published with permission of W. B. Saunders Company).

groups, based primarily on anatomic location, are as follows: 1. Anomalies which occur in the preauricular areas and are known as preauricular pits, cysts, or fistulas. These have also been called "sinus preauricularis congenita," "branchial fistula in the external ear," "fistula auris congenita," and "helical fistula."[1] 2. Branchiogenous anomalies which occur anterior to the sternocleidomastoid muscle in a general linear arrangement from the mandibles to the manubrium. Clinically, such lesions are usually cysts or fistulas. While either may be present anywhere in this distribution, Ladd and Gross[2] state that cysts are prone to lie higher in the neck than the cutaneous openings of fistulas. This observation has been true in the present series.

Again, the nomenclature of these lesions in the neck is not standard; cysts have been known as lateral cervical cysts, lateral cysts of the neck, branchial cysts, and congenital cysts of the neck. Fistulas have been called lateral cervical fistulas, congenital sinuses, and persistent branchial clefts.

Embryology.—Conflicting opinions have been presented regarding the embryologic development of these congenital lesions, and there is no uniformly accepted opinion as to their exact evolution. The following explanation has been presented by Arey[3]: Five branchial arches, separated by four branchial grooves, appear in the fourth week of development of the human embryo (fig. 1A). At the level of these external groves, the developing pharynx bulges outward from the entoderm to become the pharyngeal pouches. In the sequence of normal development, the epidermis of each groove and the entoderm of the complementary pouch meet, unite, and finally become obliterated. The anomalies discussed in this paper result from an incomplete obliteration of these grooves during the later developmental cycle.

The auricle develops around the first branchial groove, its tissue being formed by the first and second branchial arches (mandibular and hyoid). During the sixth week, six primitive hillocks appear on these parts. Earlier, it was felt that the auricle developed in a precise manner from these hillocks and from an auricular fold of the hyoid integument. Later studies are controversial; some investigators even assert that the entire auricle, except for the tragus, is of hyoid origin. Anomalous development in this region results in pits or fistulas of varying depth about the ear (fig. 1*B*).

The majority of the more caudad lesions of the neck are said to be derived from the second branchial groove. Various types of lesions result from the residuals of incompletely closed ectodermal grooves or pouches. Fistulas may communicate between the external surfaces of the neck and the pharynx; blind fistulas may lead from the pharynx or, more commonly, from the skin of the neck as a result of a persistent ectodermal groove or entodermal pouch.[3]

Results of Study

Locations of the lesions in this group of 21 patients are shown in figure 2. Lesions occurred in the preauricular areas in seven patients. In four of these, the lesions were bilateral; one had both preauricular pits and fistulas in the neck. In three instances, small preauricular pits were noted only as incidental findings in newborn infants. In the four other patients, all adults, the findings were more significant; mucoid drainage was noted from

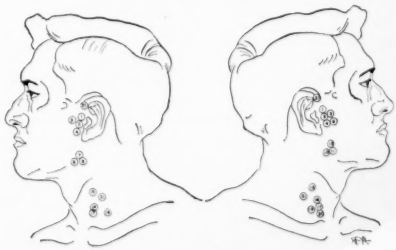


Fig. 2.—Location of congenital branchiogenous lesions in this series of patients.

one tract and purulent exudates from the others. The depth of these tracts was variable; however, in one patient the length was 5 cm. The depth was demonstrated either by diagnostic procedures or by surgical dissection. Operation was performed in three instances. Histological study of the excised material revealed stratified squamous epithelium lining the tract. The underlying rete pegs were normal, and no skin appendages were described. In

one specimen the dermis was infiltrated with neutrophils with an infiltrate of plasma cells and lymphocytes at the periphery.

Lesions in the neck were present in 14 other patients. The two clinical types seen were (1) those evidenced as firm, freely movable cysts and

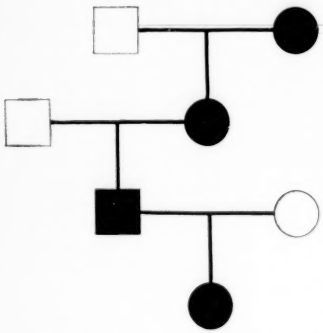


Fig. 3.—Diagrammatic history of family with branchiogenous anomalies of lower neck, showing evidence in three generations.

(2) those with openings on the skin of the neck with associated fistulous tracts.

Cystic lesions in the neck were observed in seven patients. All of these occurred at the angle of the mandible, except in the patient in case 18, in whom the tumor was located just above the mid-third of the clavicle. The cystic structures were unilateral, freely movable, and nontender, and they varied in diameter up to 5 cm. In one patient, rapid growth of the mass was noted, and various diagnoses, including parotid tumor, lymphatic tumor, and aberrant thyroid gland, had been entertained. In five patients the cysts were surgically excised, and histological examination showed stratified squamous epithelium lining the cysts and lymphoid tissue which contained well-defined germinal centers.

There were fistulous lesions with openings in the neck in the other eight patients, with only two showing bilateral orifices. These lesions tended to be present in the lower third of the neck. The orifices varied in appearance from small asymptomatic pinpoint openings to an inflamed, tender, swollen mass which, in one patient, suggested a furuncle; hyperpigmentation about the ostia was common. Drainage was mucoid in two and frankly purulent in six patients. Periodic drainage was described by three patients in whom symptoms of tenderness and pressure were relieved when the tracts were evacuated.

Surgical excision of the tracts was performed in six patients. These tracts were often in close proximity to major deep neck structures, such as the carotid arteries and jugular veins, and required careful dissection for their removal. In two instances the tracts, after complete dissection, were shown to terminate adjacent to the pharynx; in one, a pharyngeal opening was demonstrated.

In summarizing associated anomalies in this group of 21 patients, one individual had both bilateral preauricular pits and sinuses in the neck and was the only patient showing multiple branchiogenous anomalies at several levels. Among those patients with preauricular lesions, other anomalies noted were multiple hemangiomas of the hand and forearm in one newborn infant, a deformed auricle in one, and bilateral perceptive deafness in three. While several reports confirm the presence of heredity factors in preauricular lesions, none was noted in our group. In the group of 14 patients with branchiogenous anomalies in the neck, however, 3 gave a family history of this condition occurring over several generations. The diagnostic history of one family is presented in figure 3. No other anomalies were observed in this group.

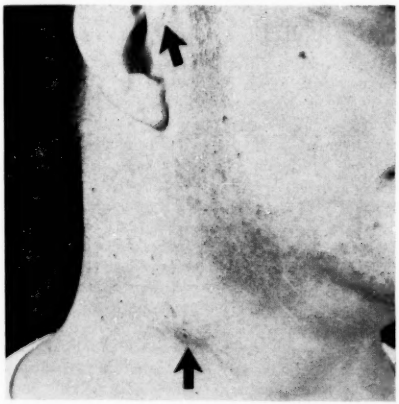


Fig. 4 (case 1).—Branchiogenous anomaly with sinuses in lower neck and pits anterior to helix.

Report of Cases

Case 1.—A 21-year-old man was admitted to Walter Reed Army Hospital on Sept. 23, 1953, with a complaint of partial deafness which had existed since birth (fig. 2, no. 21). He also described repeated troublesome infections occurring in small sinuses in his mid-neck. A family history of deafness in the patient's father and paternal grandfather was given, and there was a history of "cysts of the neck for several generations." On examination, two symmetrical draining sinuses

were found in the mid-neck along the medial border of the sternocleidomastoid muscle (fig. 4). A mucoid discharge could be expressed from these areas. Symmetrically placed ostia were also present on the anterior helix of both ears, and there was intermittent drainage from these sinuses. The

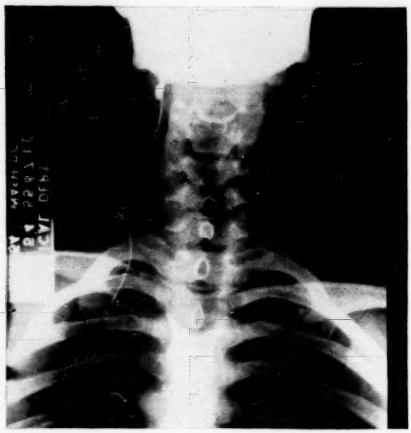


Fig. 5 (case 1).—Roentgenogram with delineation and extent of tract shown by iodized oil (Lipiodol)–filled polyethylene tube.

lesions on the anterior helix and in the neck were diagnosed as multiple congenital branchiogenous anomalies. During the patient's hospitalization the deafness was found to be bilateral and of undetermined origin. Initially, a Maico air-conduction hearing aid was fitted for the left ear in October, 1953, and one month later a contact dermatitis, apparently due to the hearing mold, developed. This was associated with secondary infection of the external ear and of the preauricular sinuses. These complications subsided on symptomatic treatment, and the patient was later discharged.

The patient was readmitted March 12, 1954, with a history of recurrent dermatitis with secondary infection about the ear, apparently due to the hearing mold. The fistulas of the neck were draining, and Staphylococcus pyogenes var. aureus resistant to penicillin but sensitive to other antibiotics was isolated.

Roentgenographic studies of sinus tracts of the neck with use of iodized oil (Lipiodol) revealed a branchiogenous fistula beginning on the level of C-5 on the right, extending slightly medial to the angle of the jaw, and appearing to end at about the base of the neck laterally. A subsequent x-ray of the soft tissues of the neck after catheterization of the sinus on the left showed a polyethylene tube, filled with iodized oil, which extended from the clavicle on the left superiorly with a concentration of the contrast medium extending into the pharynx at the level of C-2 (fig. 5). On June 9, 1954, with the patient under general endotracheal apesthesia, the right tract was surgically excised. This tract was noted to pass in close proximity to the external and internal carotid arteries anteriorly and was followed to the pharyngeal wall. The left tract was removed from a similar area. After operation, hemorrhage developed about the wound in the neck, which resulted in respiratory difficulties with laryngospasm. This was sufficiently severe to require a tracheotomy on June 10, at which time a large clot of blood was evacuated from the wound. After this procedure, the patient made a gradual but uneventful recovery.

Pathological studies of the dissected tracts revealed tubular structures which were lined, in some portions, with stratified squamous epithelium and, in other areas, by pseudostratified ciliated columnar epithelium. The surrounding tissue was densely infiltrated with lymphocytes to form lymphoid aggregates.

Prior to the patient's discharge on Sept. 17, 1954, hearing molds, made of another plastic material so that wearing could be alternated, were fitted to each ear of this patient.

Case 2.—A 22-year-old man (fig. 2, no. 20) was admitted on Jan. 23, 1952, with a sinus, on the right side of his neck, which had been draining purulent material intermittently for as long as he could remember. There was no family history of similar lesions.

Examination showed a small elevation on the right side of the base of the neck with a central opening and mucopurulent drainage. This orifice communicated with a palpable sac extending upward on the right side. This appeared adherent to the deeper structures above, since it retracted when the patient swallowed. The thyroid gland was not palpable. To determine the depth of the tract, iodized oil was instilled and roentgenograms were made (fig. 6). These demonstrated that the tract extended from the right supraclavicular area at the level of D-2 to the level of C-3. The inferior end com-

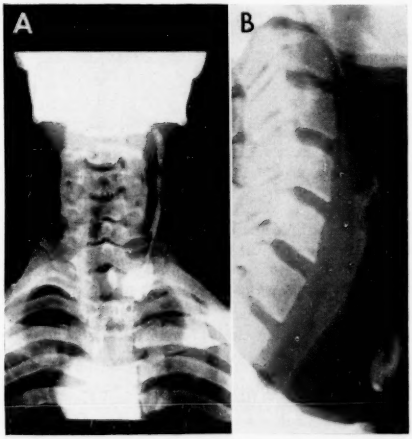


Fig. 6 (case 2).—Roentgenograms showing iodized oil (Lipiodol)–filled tract: *A*, anteroposterior view and, *B*, lateral view.

municated with an ovoid cystic structure located superficially in the anterior portion of the neck at the level of D-1 or D-2. A diagnosis of branchiogenous sinus was made.

In February, 1952, with the patient under general endotracheal anesthesia, the entire fistula was dissected (fig. 7). It was shown to extend for a distance of approximately 7 cm.,

lying between the external and internal carotid arteries and extending to the palatine tonsil. Histological examination revealed a sinus tract lined with ciliated columnar epithelium.

Comment

Branchiogenous anomalies are of interest because of the varying clinical pictures they present after secondary infection or occlusion. In some patients, the drainage from an apparently insignificant orifice may cause pyodermas or infectious eczematoid dermatitis in the surrounding skin. Such lesions may simulate granulomas or carcinomas. Other fistulas may become occluded and form cysts which may become secondarily infected, or, in some instances, they may enlarge sufficiently to produce pressure symptoms.

Although the diagnosis of a branchiogenous anomaly may be evident, at times it is difficult to evaluate the depth or extent of the associated tract, which can vary in length from 1 to 10 cm.

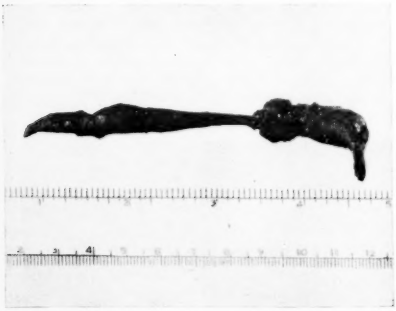


Fig. 7 (case 2).—Dissected fistulous tract.

and occasionally extend as through-and-through (skin-to-pharynx) sinuses. These sinuses may have divergent offshoots and vary in the character of their linings from stratified squamous and columnar epithelium to nonspecific fibrous tracts. In the neck, they often lie in close proximity to important deep structures, such as the carotid vessels and jugular veins.

In their differential diagnoses, Neel and Pemberton [4] include tuberculous and nontuberculous lymphadenitis, other infectious processes, tumors of the carotid, hygroma, dermoid cysts, lipomas, neurofibromas, hemanginomas, and lymphangiomas.

The association of branchiogenous anomalies with other congenital anomalies noted in this reported series has been observed previously by other authors,[5] as has the hereditary history obtained in some cases.[6]

Adequate diagnostic studies should be carried out to evaluate these lesions prior to treatment. In order to determine their extent, procedures should include careful probing or installation of radiopaque material followed by radiography. It may also be necessary, when attempting dissection, to delineate the tracts with a stain, such as methylthionine chloride (methylene blue).[7] The details of surgical techniques used in the treatment will not be described, but it is important to emphasize that thorough surgical evaluation and competent extirpation should be carried out. Inadequate treatment of these lesions by sclerosing agents, such as phenol, or by incomplete electrosurgical measures often result in partial obliteration of these tracts with subsequent secondary infection and unnecessary scarring and disfigurement.

Summary

Among a group of 21 patients with congenital branchiogenous anomalies studied at Walter Reed Army Hospital from 1950-1955, preauricular pits and fistulas were present in 7; in the other 14 patients, lesions occurred as cysts usually at the angle of the mandible or as fistulas in the lower one-third of the neck. Complications from branchiogenous anomalies result from secondary infection or from pressure. It is necessary to differentiate these lesions by adequate studies from benign and malignant tumors or from chronic infections. When treatment of these lesions is required, thorough surgical extirpation is indicated rather than a method which would result in incomplete obliteration of the tract.

The Medical Illustration Section, Walter Reed Army Hospital, and the Armed Forces Institute of Pathology supplied some of the photographs used in this paper.

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RADIATION THERAPY FOR STOMA ULCER OCCURRING AFTER SUBTOTAL GASTRECTOMY

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The effectiveness of roentgen radiation in depressing or abolishing glandular secretion can be turned to account in producing achlorhydria for therapeutic purposes. Duodenal ulcers occurring opposite the stoma after Billroth 2 operations were studied in 23 patients. In order to reduce the secretion of acid by the gastric remnant, it was irradiated, generally with supervoltage x-rays (2 mev.). The tissue dose was approximately 1,800 r in all cases. The resulting reduction in gastric acidity was variable and unpredictable, but analyses showed that achlorhydria or pronounced hypochlorhydria was present in more than half of the patients up to two years after irradiation. Clinically satisfactory results were obtained in 15 patients after one course of therapy. Experience indicated that patients in whom the achlorhydria persisted for three years were unlikely to have further ulceration or to need additional surgery.

In the surgical treatment of duodenal ulcer, any operation which joins gastric mucosa to the mucosa of the small intestine may be followed in an appreciable proportion of cases by an anastomotic ulcer; subtotal gastrectomy provides no exception to this rule.

Although it is generally accepted that subtotal gastrectomy with use of a Billroth 2 type of anastomosis has resulted in a lower incidence of recurrent ulcer than the Billroth 1 resection, hemigastrectomy, or gastroenterostomy, the number of stoma ulcers occurring after high resection is large enough to be significant. In a 10-year follow-up study of 351 consecutive patients with duodenal ulcer who were subjected to the Billroth 2 subtotal gastrectomy, anastomotic ulcers developed in 6.6%.[1]

Stoma ulcer occurring after operation is a serious clinical development which usually presents a much more difficult therapeutic problem than the primary duodenal ulcer. Conventional medical treatment with antacids and anticholinergic drugs may relieve symptoms as long as the patient is at rest, but when normal activity is resumed symptoms and signs of active ulceration are likely to recur.

Evidence that the surgical treatment of gastrojejunal ulcer is not satisfactory may be found in the report of Walters and associates.[2] In patients with recurrent jejunal ulcer after gastric resection, vagotomy produced achlorhydria in only one-half and the clinical results were unsatisfactory in 30%. Resection of the anastomosis and a portion of the remaining gastric stump combined with a subdiaphragmatic vagotomy appeared to give the best surgical results. However, this is a formidable procedure to recommend to a patient who has already gone through a major operation for relief of ulcer, and any further reduction of the size of the gastric stump may prove to be a serious handicap to the patient's nutrition after a second operation.

There is clinical evidence that the postoperative development of a stoma ulcer is in itself an indication that the ulcer diathesis in the patient is so strong that peptic ulceration will occur unless a sustained and complete achlorhydria has been achieved. In patients who were subjected to resection for stoma ulcer occurring after a previous operation, a second stoma ulcer developed in 14.5%—more than twice the incidence observed in patients operated on for duodenal ulcer.[1] Cases have been reported in which ulcers recurred after all but a tiny remnant of stomach had been removed, but most clinicians will agree that total gastrectomy is too radical a surgical procedure for a benign condition. It is generally agreed that postoperative ulceration is dependent on the persistence of free hydrochloric acid in the secretions of the gastric stump, and all therapeutic plans have as their objective either the neutralization or the elimination of the acid factor.

The idea of using radiation in a deliberate attempt to produce gastritis and thereby reduce gastric secretion in cases of duodenal ulcer was first suggested in 1909 by Bassler.[3] Bruegel [4] in 1917 and Holman and Lewis [5] in 1941 reported on the use of irradiation of the stomach in the treatment of duodenal ulcer. During the last 10 years several studies have been made on the value of gastric irradiation in the treatment of peptic ulcer.[6]

The amount of radiation generally used has ranged from 1,600 to 2,000 r delivered into the stomach. The reduction in gastric acidity produced by these dosages is variable and unpredictable, but

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as a rule the acidity begins to diminish in two to four weeks after irradiation, continues to decrease for several weeks or months, and then tends to return gradually to the same level as before treatment. Achlorhydria develops in about 12% of patients but may be transient. In the majority of patients, pretreatment levels of acid secretion have been resumed in about two years.

By gastroscopic and serial biopsy methods, the degree of inflammation of the gastric mucosa has been shown to parallel the effect on secretion.[7] Acute irradiation gastritis develops, reaches a peak of severity, and then subsides—the mucosa in most cases returning to normal without fibrosis. In a few instances, some atrophy persists and prolonged hypochlorhydria or achlorhydria then is usually present. Although present evaluations indicate that irradiation therapy is best considered as an adjunct to conventional treatment of duodenal and gastric ulcer, it may well be more applicable in the management of stoma ulcer after subtotal gastrectomy.

Clinical Material and Methods

Clinical Material.—This report is based on our experience with the use of supervoltage x-ray therapy in 23 patients with stoma ulcer after subtotal gastrectomy. Since the series is small and the follow-up period less than two years in the majority of cases, this paper must be considered a preliminary report. Further long-term observations are necessary for final evaluation of the method.

Only 1 of the 23 patients was a woman. Twelve had undergone gastric resection at the Lahey Clinic, and 11 had been operated on elsewhere. In every case gastric resection with a Billroth 2 type of anastomosis had been used, and in only one did x-ray examination indicate that less than 70% of the stomach had been removed. In seven cases the gastric resection had been carried out in an attempt to cure a stoma ulcer which had occurred after a previous operation. In four cases vagotomy had been performed. Eight patients had been hospitalized for a trial of medical treatment which was unsuccessful.

Diagnosis.—In 18 of the 23 patients an ulcer crater on the jejunal side of the anastomosis was demonstrated by x-ray examination. In the remaining five, the only objective evidence of ulcer was hemorrhage from the gastrojejunal area. Free hydrochloric acid was demonstrated in the gastric secretions before treatment in all but one patient, and in this patient only one examination was made. Inherent difficulties in gastric analyses after gastric resection make repeated tests necessary to determine the true level of secretion. A high level of free acid may be considered extremely significant in the diagnosis of recurrent ulcer.

Our method of obtaining gastric juice from the resected stomach was to keep the patient lying flat in the supine position with the tip of a Levin tube in the fundus. A fractional analysis was made with use of either Ewald's test meal or histamine as a stimulant. The sample showing the highest titer of acidity was considered to be the significant specimen. A high level of acid secretion by the gastric remnant was the rule in the 18 patients in whom a crater was demonstrated by x-ray; the free acidity was 20 degrees or over in 12 and 40 degrees or over in 5. In the five patients without demonstrable crater the free acidity was 20 degrees or over in two.

Technique of Irradiation.—Of the 23 patients, 2 were treated by Dr. Joseph Marks at the New England Deaconess Hospital, Boston. One of these was given a second series of treatments at the Massachusetts Institute of Technology three months later. Dr. Marks used 2 mv. of x-ray and the same essential technique as was used by us. Three patients were treated with 400 kv. of x-ray, half-value layer 3.8 mm. Cu, in our radiology department at the Lahey Clinic. All the other treatments were carried out at the Massachusetts Institute of Technology, with 2 mv. of x-ray, half-value layer 12.8 mm. Cu at a target midplane distance of 125 cm. This was part of the cooperative program between the Lahey Clinic and Professor John G. Trump and his associates.

The tissue dose was approximately 1,800 r in all cases. The three patients treated at the clinic with 400 kv. of x-ray received approximately 1,700 r. The plan of therapy is to give a tissue dose of 180 r five times weekly for two weeks, or 10 treatments. Anterior and posterior fields are used on alternate days. The patients are in a standing position, and, since we wish to treat only the gastric stump, field sizes usually do not have to be larger than 10 by 10 cm. provided the localization is accurate. We consider the localization of portals highly important, and in our opinion one of the prime factors in producing poor results after x-ray therapy is lack of proper localization of the x-ray beam.

Results

Acid Secretion.—Because most of these patients lived some distance from Boston, it was impossible to check the gastric acidity at regular fixed intervals. In all but four, however, gastric analyses were made at irregular intervals after treatment. Altogether, 42 gastric analyses were carried out on 19 patients during the first two years after treatment. There was one during the third year and one during the fourth year. In all but one instance, the free acid titer was well below the free acid figure in that patient before irradiation. The tabulated results (see table) show that achlorhydria or pronounced hypochlorhydria was present in over one-half of the patients up to two years after irradiation.

In 10 patients tested within the first two months after x-ray therapy, the level of free acid was found to be reduced in comparison with the pretreatment figure. The free hydrochloric acid level was 5 units or less in three patients, and in three achlorhydria

Gastric Stump Acidity After Radiation Therapy

	Period After Therapy, Mo.			
	2	2-6	6-12	12-24
Not tested, no.	10	12	10	10
Free HCl below pretreatment level, no.	10	11	10	10
Less than 5 units of free HCl, no.	3	1	0	2
Achlorhydria, no.	3	5	5	6

was present. In 12 patients tested during the following four months (the period from two to six months after therapy), the free acid level was reduced in all but one. It was less than 5 units in one, and achlorhydria was present in five. In 10 patients tested during the second six-month period after therapy, the free acid level was reduced below the pretreatment level in all. Achlorhydria was present in five; three patients had 10 units, and two had 25 units of free hydrochloric acid. In 10 patients tested during the second year after irradiation the free hydrochloric acid level was well below the pretreatment level in all. Two patients had less than 5 units, and achlorhydria was present in six.

Fig. 1.—Roentgenogram of anastomosis between gastric stump and jejunum, showing ulcer crater (*arrow*) in jejunum just distal to stoma. *Insert*, spot view of stoma and crater.

The results obtained in this small group of patients give some hopeful indication that the recovery of acid-secreting power of the fundal stump is not as likely to occur as it is in the case of the irradiated intact stomach and that, if achlorhydria or nearly complete achlorhydria is once established, it may persist.

Ulcer Crater as Visualized by X-ray.—In 18 of the 23 patients, the pretreatment diagnostic evidence included the demonstration of an anastomotic crater by x-ray. In 12, diagnostic x-ray studies after treatment showed that the crater had healed. In two others the crater disappeared only after a second course of irradiation treatment. Two patients lived too far away to return for follow-up x-ray studies but reported that they were symptom-free one and one-half and eight years, respectively, after treatment. In the two remaining patients, craters were found 34 and 36 months after treatment. Both of these patients had been symptom-free for almost three years, which would suggest that the primary crater had initially healed but subsequently recurred.

Fig. 2.—Roentgenogram of anastomosis between gastric stump and jejunum four months after irradiation therapy, showing smaller mucosal folds and no ulcer crater.

In some instances a post-treatment x-ray examination carried out less than two months after irradiation showed that the crater was still present but reduced in size; these craters subsequently disappeared. Figures 1 and 2 show x-ray evidence of the healing of a stoma ulcer after irradiation of the gastric stump. The observations on 18 patients in whom anastomotic craters were demonstrated before treatment indicate that these craters consistently heal if gastric acidity is abolished by one,

two, or three courses of irradiation therapy. If the acid secretory power is recovered by the gastric stump, however, a new crater may form.

Hemorrhage But No Demonstrable Crater.—Five patients were treated for recurrent hemorrhage after subtotal gastrectomy. They had persistently high levels of acid secretion but no demonstrable ulcer crater. In three of these cases the hemorrhages were multiple. In one patient with an 8-month follow-up study and two with 15-month follow-up studies, achlorhydria was produced and no symptoms have been reported. In one, achlorhydria was not achieved and further hemorrhages occurred until a second course of irradiation was given. Although no further hemorrhage has occurred in the fifth patient, a second course of therapy was given because of persistent acid secretion and some distress.

Relief of Pain.—In 17 of the 23 patients, pain was a prominent symptom before therapy. Pain was relieved in all but three by one course of irradiation. Two of these three patients with persistent pain were eventually relieved after a second course. In one patient, complicating pancreatitis caused pain which persisted for three months after therapy.

Recurrence.—Of the 23 patients treated, 16 have had a follow-up period of less than two years. Eleven of these are still symptom-free and show no evidence of recurrence after one course of therapy. One patient had a recurrent or persistent crater, and hemorrhage occurred in one, and mild pain in another. Further irradiation was given in all three of these patients, and they are now symptom-free. The two remaining patients have died of intercurrent disease.

Seven patients have had follow-up periods of two to eight years. Four of these have remained symptom-free, and in all four the free hydrochloric acid level in the gastric secretions is either absent or very low. In the remaining three, recurrent hemorrhage, pain, and crater formation have occurred from three to five years after therapy. Thus, the present status is satisfactory after one course of therapy in 15, satisfactory after two or three courses in 3, and unsatisfactory because of recurrence in 3. Two died from intercurrent disease.

Side-effects.—No important side-effects were observed in this group, even though two courses of treatment were given in three cases and three courses in one. Four patients complained of some nausea during the treatment. Epilation was noted in one patient, and slight erythema has been observed in several. In one patient who was treated for multiple hemorrhages, some bleeding occurred during the treatment.

No definite evidence of any injury to other organs in the treated area has been noted. Diabetes developed a few months after treatment in one patient, but there was evidence of pancreatitis before therapy. One patient was subjected to left nephrectomy for renal cell carcinoma two years after receiving two courses of irradiation; he later died of metastases. The relationship between the radiation therapy and the subsequent development of carcinoma of the left kidney is a matter for conjecture.

Summary and Conclusions

In 23 patients treated with irradiation, clinically satisfactory results were obtained in 15 after one course of therapy. The results in three other patients were clinically satisfactory after a second or third course of irradiation. In three patients, results must be classified as failure because of recurrence of stoma ulceration, but in all three the supervision was inadequate and there was no opportunity to repeat or supplement the treatment before severe signs and symptoms developed. Two patients died of intercurrent and unrelated disease.

Radiation doses of 1,800 r with 2 mv. of x-ray can be administered to the stump of the resected stomach and, if necessary, repeated one or two times at intervals of six months without serious danger or untoward side-effects. Adequate radiation therapy materially and consistently reduces the secretion of hydrochloric acid, and, if achlorhydria is established, relief of pain and healing of the anastomotic ulcer occur.

Because the suppression of gastric secretion is not always complete or permanent, follow-up studies should be carried out in patients receiving this form of therapy and examinations made for recurrent ulcer or acid secretion; further treatment should be instituted if either condition is found. There is evidence that, if achlorhydria persists for three years after treatment, no further ulceration is to be expected.

In patients with anastomotic ulcer or gastric hemorrhage associated with persistent secretion of gastric acid occurring after subtotal gastrectomy for duodenal ulcer, irradiation of the gastric stump is a safe, rational, and effective treatment which may obviate the need for additional major surgery.

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The Massachusetts Institute of Technology supplied the 2 million-volt radiation sources and assumed responsibility for physical aspects in this study.

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ETIOLOGY OF DUODENAL ULCER

II. SERUM PEPSINOGEN AND PEPTIC ULCER IN INDUCTEES

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The possibility that the concentration of pepsinogen in the blood serum might be correlated with other measurable structural or functional characteristics was investigated in 2,262 men selected randomly at a large army induction center. Pepsinogen values were expressed as micrograms of tyrosine released by the action of 1 ml. of serum in a standard assay procedure. The mean value for 2,031 of these men was 440 units, with a standard deviation of 136. Duodenal ulcer was found in 13 men and gastric ulcer in 1; the mean pepsinogen value for the 14 men was 707 and was significantly higher than that of the group as a whole. A low positive correlation was found between the pepsinogen value and a man's position in his family in that the average value for oldest children was higher than the corresponding figures for younger or only children, but there was no significant correlation with objective measures of social behavior or over-all military performance.

The findings described in this paper are the result of a project begun in October, 1954, by the department of psychiatry at the Walter Reed Army Institute of Research. It was designed to study the development of peptic ulcer in inductees and was conducted initially at a large induction station in the eastern United States. A total of 2,262 randomly selected inductees were chosen for this study over a two-month period at the rate of approximately 300 per week, certain tests and desired items of information being made part of the routine induction procedure. A previous article by Weiner and coworkers [1] reported on some of the initial findings of this project concerning the relationship between psychological characteristics and serum pepsinogen.

The present paper presents a part of the data which have been obtained from a two-year follow-up study of the military performance and medical records of the subjects of this investigation.

A correlation between peptic ulcer and pepsinogen (both serum pepsinogen levels and uropepsin excretion) [2] and between peptic ulcer and ABO blood groups [3] has been demonstrated by current research. Consequently, among the tests chosen for this study were the pepsinogen concentration in the serum and the blood type. In addition, the Cornell Medical Index (CMI), the Saslow test, an extensive, specially designed sociological questionnaire, and photographs for analysis of the somatotypes (Sheldon) were employed. In this paper, certain sociological background data and parts of the CMI are used but the bulk of the material will be reported in separate studies later. The pepsinogen

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values were determined by the method described in the earlier paper.[1] Those individuals whose pepsinogen levels were in the upper and lower 10% of the group each week were specially coded, and a random group of these men (121 subjects, 64 with hypersecretion and 57 with hyposecretion) was selected for additional studies, such as psychological testing, interviews by psychiatrists and psychiatric social workers, and x-rays of the upper gastrointestinal tract. These x-rays were done at the time of induction, again about three or four months later, and, in 97% of the cases, again about a year after induction. The x-ray studies were conducted with special care by well-trained radiologists who were on duty in the large Army hospitals which gave diagnostic and medical service to the troops in the geographical areas to which the subjects of this study were assigned. Clearly, no method is perfect, and, hence, errors—chiefly of omission—have probably occurred. It may be noted, however,

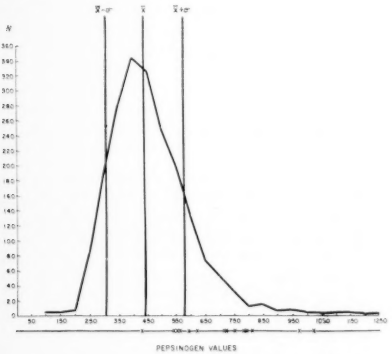

Fig. 1.—Pepsinogen level distribution curve of 2,031 subjects. Mean ($\bar{x}$) = 440; standard deviation (σ) = 136. One standard deviation above mean ($\bar{x} + \sigma$) = 557 = hypersecretion cut-off level; one standard deviation below mean ($\bar{x} - \sigma$) = 304 = hyposecretion cut-off level. Each ulcer case (X) is plotted at pepsinogen level below abscissa.

that in one subject in whom the first fluoroscopy was suggestive of ulcer, due to spasm, a total of five roentgenographic examinations were conducted with a final diagnosis of "no ulcer." When the data from the various technical studies were compared at the conclusion of the study, it was found that this man had a low serum pepsinogen level—namely, 222 units (expressed as micrograms of tyrosine released by the action of 1 ml. of serum at pH 1.5 in the standard assay procedure [4]), which is in the hyposecretion group.

No attempt was made to influence the assignment of any of the subjects in the total research sample. At the end of one year's service, information was requested from each of the 2,262 men's commanding officers as to their adjustment to military life. At the end of their two years' obligatory service, complete military records, medical as well as administrative, were obtained for each man. Consequently, we were in a position to estimate and evaluate the over-all performance and certain particular incidents for each subject during his military service. Because our population sample was composed of draft-age men, the mean age was correspondingly low—20.8 years; 96% of the group were Caucasian and 3.5% Negro. Only the aspects of this project which deal with pepsinogen, peptic ulcer, and blood groups will be reported in this paper.

Distribution of Pepsinogen Levels and Peptic Ulcer

Although the total research sample was composed of 2,262 men, pepsinogen levels were obtained on only 2,031 subjects because of unavoidable accidents, such as some samples being lost or broken in transit. The distribution of the concentration of pepsinogen in the serum of the 2,031 men is depicted in figure 1. The values ranged from 66 to 1,244 units, with a mean ($\bar{x}$) of 440 and a standard deviation (σ) of 136. Hyposecretion was defined as a pepsinogen value less than one standard deviation below the mean (i. e., 304 or below); hypersecretion was a pepsinogen value greater than one standard deviation above the mean (i. e., 577 and above).

Out of the total research population of 2,262 men, a diagnosis of peptic ulcer was made in 16. However, in two of these subjects pepsinogen values were not obtainable. Therefore, in the sample of 2,031 men, 14 cases of peptic ulcer were diagnosed during the subjects' two-year tours of duty; 13 persons had duodenal and 1 had gastric ulcer. The diagnosis of ulcer was made only if there was positive x-ray evidence of an ulcer crater or scarring secondary to an ulcer. Those with severe pylorospasm were not included.

It is to be noted that eight of the ulcer cases were discovered in the "special study group" of 121 men in whom routine gastrointestinal x-rays were obtained at our request. Five of these ulcers were detected solely by routine examination; only three subjects had upper gastrointestinal and/or ulcer symptomatology at the time the diagnosis of ulcer was made. Two of these were actually hospitalized because of ulcer, the symptoms being so marked in one case that medical separation from the service was necessary. This was the only one of the 16 patients with ulcer who was unable to complete his obligatory period of military service. All eight cases were diagnosed within four months after the subject's induction, no further ulcer cases being detected in this group during the rest of the two years' service. The remaining ulcer cases came from the rest of our research population, and all of these men received x-rays because of the symptoms which brought them to seek medical care. These ulcers were detected 3 to 15 months after induction.

The source tables of the Medical Statistics of the United States Army, Annual Report of the Surgeon General, 1954, reveal an incidence of ulcer of 3.13 per 1,000 troops for the year 1954. Therefore, the total number of ulcers (16) discovered in our series (2,262 men) over a two-year period (3.54 per 1,000 per year) approximates the expected frequency of ulcer Army-wide.

TABLE 1.—*Distribution of Blood Types in Research Population**

Blood Group	Total Population		With Ulcer		Without Ulcer	
	No.	%	No.	%	No.	%
A	853	38.4	9	56.3	844	38.3
B	291	13.1	3	18.7	288	13.0
AB	83	3.7	1	6.2	82	3.7
O	997	44.8	3	18.7	994	45.0
Total	2,224	100.0	16	100.0	2,208	100.0

* $p = 0.3$ to 0.2.

Serum pepsinogen levels in the 14 subjects varied from 427 to 1,027 units with 10 falling within the hypersecretion category (fig. 1). The one subject with gastric ulcer had a pepsinogen level of 978 units, the second highest value among those with ulcer.

The mean of the pepsinogen values for the ulcer group is 707. With use of the *t*-test, the difference between the mean in subjects with peptic ulcer and the mean in the general sample (440) was found to be significant beyond the 0.001 level of confidence. Therefore, these findings are consistent with others that show that those persons who develop peptic ulcer come from that segment of the population with high serum pepsinogen values.[5]

ABO Blood Groups

Recently a great deal of work has been reported on the relationship of ABO blood groups with various diseases, especially those conditions associated with altered acidity of the stomach, e. g., gastric and duodenal ulcer, gastric carcinoma, and pernicious anemia. Aird and associates [3a] and Clarke and co-workers [3c] in England, Køster and co-workers [3b] in Denmark, and Buckwalter and associates [6] in the United States report that there is an increased frequency in the incidence of blood group O in patients with peptic ulcer as compared with controls and an increased incidence of blood group A (with a corresponding decrease in blood group O) in patients with such lesions as gastric carcinoma and pernicious anemia. In contrast, Clarke and co-workers [3d] present data, including sibship studies, indicating no such relationship.

Out of the total research population (2,262), 16 subjects developed ulcer (by x-ray diagnosis). In 2 of these 16, serum pepsinogen levels were not obtained and therefore were not included in the description in the preceding section. The blood type, however, was known for all 16. The distribution of blood types for our research population is shown in table 1. It will be seen that this distribution is approximately the same as that usually recorded for the United States. Of the 16 subjects with ulcers, 9 were group A, 3 group O, 3 group B, and 1 AB. This would seem to show that approximately 56% of the ulcer subjects were group A, whereas only 38% of the research population were group A and only about 19% of the ulcer subjects were group O as compared with 45% of the population. However, chi-square analysis of these data were not significant. (In all the chi-square statistical analyses in this paper, a p value of 0.05 or less was accepted as the level of statistical significance.) Consequently, in our series no relationship between blood type and the incidence of peptic ulcer was demonstrated.

As has been shown, attempts have been made to correlate ABO blood groups with peptic ulcer and pepsinogen with peptic ulcer. Mirsky [7] has analyzed data regarding the relationship between ABO blood groups and serum pepsinogen levels; no correlation was found. Køster and associates [3b] compared the blood groups of patients with conditions associated with low and high hydrochloric acid secretion in the stomach (fig. 2, *left*). They reported an increased frequency of blood group O and a decreased frequency of blood group A in conditions associated with increased acid production.

In our series, there were 2,014 subjects who had both pepsinogen levels and blood types available. When each pepsinogen secretion category is broken down into the percentages of ABO blood groups within it, and plotted on a graph, it will be seen that there is a trend not unlike that reported by Køster and associates, namely, with increasing pepisongen levels there is an increased frequency of blood group O and a corresponding decrease in blood group A (fig. 2, *right*). Blood groups B and AB show no such trend. However, plotting the blood

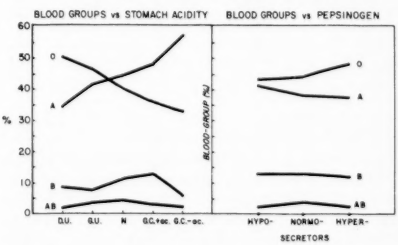

Fig. 2.—*Left*, frequency of ABO group in five different conditions of the stomach, ranging from hyperacidity to achlorhydria.[3b] (D. U. = duodenal ulcer, G. U. = gastric ulcer, N = normals, G. C. + ac. = gastric carcinoma without achlorhydria, G. C. − ac. = gastric carcinoma with achlorhydria.) *Right*, frequency of ABO groups compared with pepsinogen secretion categories in 2,014 Army inductees.

groups against secretor categories and analyzing these data by means of the chi-square test revealed no significant relationship. Consequently, the slight trend cited cannot be interpreted.

Pepsinogen and Behavior

The demonstrated relationship of high serum pepsinogen level and personality factors to the incidence of peptic ulcer, together with the evidence for the genetic determination of the level of serum pepsinogen,[5] raises the question of a possible relationship between serum pepsinogen level and personality factors. A relationship between "stress" and urinary excretion of uropepsin [8] further suggests a possible correlation of psychological and organic factors.

In the first publication from this project—analyzing the psychological data obtained on the "special group" of subjects with high and low pepsinogen secretion in our population sample—Weiner and co-workers [1] found a significant correlation between serum pepsinogen level and personality characteristics. The data used were the responses of the subjects to a battery of psychological tests, consisting of a group Rorschach, Blacky pictures, and Draw-a-Person test and, in addition, certain items of the Cornell Medical Index and Saslow test. They concluded that persons with hypersecretion showed intense "oral" needs, such as wishing to be fed, to lean on others, and to seek close bodily contact with others; if attempts to gratify these needs fail the resultant frustration causes anger which cannot be expressed for fear of a loss of the supply of these needs. They also felt that persons with hyposecretion had less problems of dependency but were more narcissistic, showing more problems relating to bodily discomfort and reacting to sources of discomfort with freely expressed hostility, some even showing hostile feminine identification which they defended themselves against by a masculine overcompensation.

TABLE 2.—*Relationship of Social Behavior and Background Factors to Pepsinogen Levels*

Behavior	p Value	Significant
Social (Performance)		
Final military performance rating	0.3-0.2	No
Court martial convictions	0.2-0.1	No
Court martial offenses	0.1-0.05	No
Number of times AWOL	0.5-0.3	No
Civil criminal record	0.7-0.5	No
Type of discharge	0.02-0.01	Yes
Medical		
Symptoms or complaints at induction		
CMI total "yes" responses	0.95-0.9	No
CMI stomach complaints only	0.5-0.3	No
Pathology, treatment, etc.		
Peptic ulcer	0.001	Yes
Treatment for other GI complaints	0.5-0.3	No
Outpatient medical record	0.5-0.3	No
Hospitalization		
History of any	0.7-0.5	No
Number	0.7-0.5	No
Days	0.1-0.05	No
Reason (GI or other)	0.2-0.1	No
Social Background		
Broken home	0.95-0.9	No
Age of broken home	0.10-0.05	No
Position in family	0.05-0.02	Yes
Social class affiliation	0.9-0.8	No

Every individual was given an over-all performance rating for his military service by two officers conjointly (by one of us [P. G. Y.] and a psychiatric social work officer who had considerable past experience in commanding troops). The performance ratings given were (1) above average, (2) average, (3) below average, (4) failure, and (5) separately classified. (The details of this rating system, as well as the whole problem of performance and military effectiveness as it relates to numerous variables, is the subject of a separate study now in preparation based on this population sample.)

In order to be given an "above average" rating, a soldier had to have demonstrated clearly outstanding performance in a major duty assignment. A rating of failure was given when the subject failed to complete his obligatory period of military service because of such things as having received a medical discharge or discharge by a court martial or through administrative channels for unsatisfactory behavior. A fifth rating included such categories as hardship discharge and erroneous induction. This fifth rating was not included in the analysis, and the total number of subjects on whom the relationship of blood pepsinogen level to performance was based was, therefore, 1,999.

The average and below-average ratings were arbitrarily determined with the general principles utilized in the previous study on military effectiveness by Glass and associates.[9] In keeping with such studies, the performance of this sample showed that approximately 90% rendered satisfactory service (average and above-average ratings) and only about 3% were failures. From the performance standpoint then, this sample is a representative one. When these military performance ratings were compared with the pepsinogen categories and the data analyzed by means of the chi-square test, no significant relationship was found.

Table 2 shows the level of significance (p value) from the chi-square test of the relationship of the items of social behavior and social background

It is to be noted that the data used by Weiner and co-workers were directed toward defining personality characteristics but not toward describing overt behavior or predicting performance. Indeed, the results of the studies by Glass and associates [9] clearly indicate that a wide spread of personality characteristics is compatible with adequate to superior performance in a military situation. In order to investigate these questions further, possible correlations between the serum pepsinogen levels of our subjects were compared with data on military performance (1,999 subjects) and also with certain arbitrarily chosen items of social background (table 2).

which have been selected for comparison with serum pepsinogen levels. No significant relationship was found except for the type of discharge, presence of peptic ulcer, and position in family.

The relationship of the incidence of peptic ulcer, as already described, is highly significant. The item "type of discharge" refers to discharge from the Army for (1) completion of tour of duty, (2) medical reasons, and (3) administrative discharges, bad conduct discharges, or similar reasons. The low significance noted in the table was due to the fact that medical discharges (not for ulcer) were slightly higher in the hyposecretion group than would have been expected by chance distribution. Analyses of those discharges that reflect aberrant social behavior (i. e., administrative discharge) fail to show any relationship to pepsinogen level.

Except for peptic ulcer, items reflecting medical behavior (CMI, outpatient treatment, and hospitalization) failed to correlate with pepsinogen values. Whether a person was hospitalized or not, the number of hospitalizations, days of hospitalization, and the reason for hospitalization (i. e., for upper gastrointestinal complaints other than ulcer, compared with all other reasons combined) all fail to show any significant relationship to the serum pepsinogen values.

In the age group of this population it is clear that, other than peptic ulcer, the criteria for medical problems and the criteria for over-all military performance show practically no significant relationship with pepsinogen secretion categories. These results again emphasize the previously reported and generally accepted conclusion that subjects of widely varying personality characteristics or psychological make-up perform equally well in the over-all military requirements. The significant relationship of serum pepsinogen level to peptic ulcer is in striking contrast to all the other criteria examined.

Of the items of social background chosen, only the position in the family (oldest child, youngest child, only child, and other) shows a statistically significant relationship to serum pepsinogen level, the results of chi-square analyses of the data yielding p values of 0.05 to 0.02. An analysis of variance was performed on the frequency distribution of pepsinogen values in each of the four categories of position in the family. The F value resulting from this analysis was significant beyond the 0.05 level of confidence. Figure 3 shows the means for the position in family, and it will be seen that the rank order of these means (from highest to lowest) are oldest child, other child, youngest child, and only child. When *t*-tests were computed to compare the various pairs of means, it was found that the difference between the mean for the oldest child and the only child was significant at the 0.02 level and the difference between the oldest and youngest child was significant at the 0.05 level. The difference between oldest and other child was not significant.

The small absolute differences between the means of these groups and the possibility of a chance finding of a significant relation in any long series of tests of complex data suggest that this finding is not of practical importance and indeed may not be supported by further studies. One reason, however, for considering these data is that the rank order may be related to cultural attitudes not infrequently encountered in families of different size. Thus, the oldest child may experience a continuing state of responsibility combined with frustration in contrast with a state of "baby" of the family (youngest child) or of lack of competition for immediate "rewards" (only child). It may, therefore, be desirable in future studies to obtain childhood developmental data for comparison with serum pepsinogen levels. Such data would further clarify the problems of the reciprocal relationships between somatic and psychological factors and their propensity for modification by life experiences.

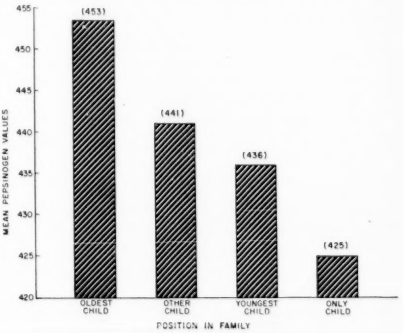

Fig. 3.—Rank order of distribution of mean pepsinogen values and position of child in family in 1,755 Army inductees.

Summary

The serum pepsinogen values found in 2,031 inductees ranged from 66 to 1,244 units. The mean was 440, and the standard deviation was 136. Hyposecretion was defined as a pepsinogen value less than one standard deviation below the mean and hypersecretion as pepsinogen values greater than one standard deviation above the mean.

Fourteen of these subjects developed peptic ulcer in the Army; 10 showed hypersecretion, 3 just below the cut-off point and only 1 as low as the mean of the total group. The mean pepsinogen value for the ulcer group was 707, and the difference between this and the mean of the total sample was significant beyond the 0.001 level of confidence.

No significant relationship between blood type and either peptic ulcer or serum pepsinogen was demonstrable. Pepsinogen levels failed to correlate with over-all military performance or other items chosen as objective measurements of social behavior. A slight positive relationship was found between position in the family and pepsinogen, the oldest child tending to have higher pepsinogen values than younger or only children.

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MSP H. A. Becker provided assistance in collection, coding, and analysis of these data. Statistical analyses were performed with the aid and supervision of Capt. H. A. Williams (MSC).

OUTWITTING ANTIBIOTIC RESISTANCE.—At Liverpool it has been customary in the past four years to treat male patients suffering from gonorrhoea with single injections of 0.5 g. of streptomycin. The numbers so treated were 215 in 1954, 231 in 1955, and 241 in 1956, and the results have been good. Nevertheless the proportion of failures increased from 2.3% in 1954 to 4.9% in 1955 and 7.0% in 1956. Alergant, who reported these facts, had not attempted to demonstrate streptomycin resistance in vitro, but had little doubt that streptomycin-resistant strains of the organism were emerging. Curtis and Wilkinson in London, found only 1 streptomycin-resistant strain of gonococci among 81 tested; and Cradock-Watson et al., also in London, found none resistant among 200 tested. The evidence suggests, therefore, that development of resistance is related to the local practice with penicillin-resistance in London where penicillin has been the drug of choice and streptomycin-resistance in Liverpool where streptomycin has been the routine remedy. Further data are required, especially on tests in vitro in Liverpool; but these findings may point the way to a means of dealing with this difficult problem. The evidence is scanty; but, such as it is, it suggests that sensitivity may perhaps be restored if the drug is withheld from patients with the infection. Dunlop showed that 86% of cases of acute gonorrhoea seen at the London Lock Hospital in 1946-47 were resistant to treatment with sulphonamides; but Cradock-Watson et al., who tested their 200 strains of gonococcus for sensivity to sulphathiazole, found to their surprise that 199 of them were inhibited by 8 mg. or less sulphathiazole per 100 ml. A concerted policy of changing from one remedy to another in selected areas, at agreed intervals, might help to preserve the efficacy of these drugs; but much more information is required before such a plan can be advocated with confidence.—Annotations, The Treatment of Gonorrhoea, *The Lancet*, October, 1958.

THE SINGLE SEIZURE—ITS STUDY AND MANAGEMENT

Madison H. Thomas, M.D., Salt Lake City

It is impossible to tell whether a single convulsive seizure occurring in a given patient is destined to be his only seizure or whether it will prove to have been the first of a series. A study is made of 48 single or first seizures in patients who ranged in age from 2 to 66 years in an effort to identify factors that might have prognostic value. Of the 48, 13 had subsequent attacks. Thus, a single seizure should not be taken lightly, and an aggressive program of neurological and electroencephalographic diagnosis is called for. In some instances the diagnosis clearly calls for medical or surgical treatment, but in general the 27% likelihood that there will be at least one more seizure justifies anticonvulsant medication. If the patient is kept free from seizures for two years, it may be safe to carry out a gradual termination of the medication.

The single seizure presents a problem as old as any in the field of epilepsy. There are many persons who have had a single seizure and never had a recurrence. Each of the million or more patients with known recurrent seizures must have had such an initial attack, and the physician, at that time, had no way of knowing what the future course would be. With increasing public education and wider recognition of epilepsy, we will have increased opportunities to see persons after these initial attacks.

However, if one consults the average medical library for guidance, one is surprised to find relatively little help available on this point. Almost all textbooks of medicine, neurology, or pediatrics define epilepsy as a "recurrent illness" and remain silent on what to do while waiting for it to become recurrent. A few more recent references consider the problem briefly and often with divergent conclusions. Because of these uncertainties, I will review these points of view and outline some preliminary observations in a longer range follow-up study of patients first seen after a single seizure episode.

Occurrence of Single Seizures

The term seizure, or epileptic seizure, encompasses a variety of patterns signaling different things to the observer. From the practical point of view, most patients with single seizure problems will have a grand mal attack or more protracted focal motor or psychomotor attack. Cases of petit mal, subjective sensory, or brief psychomotor attacks will seldom be witnessed by an observer astute enough to bring the patient to a doctor's attention.

As is true throughout medicine, we cannot forecast the future for an individual person, but we can learn about it and be guided to probable patterns by experience with others with the same or related problems. For example, Lennox has observed an incidence of seizures in 5% of all children under 5 years of age, one-half of these being related to febrile illnesses. Livingston found that 5% of patients with this type of febrile convulsion later had chronic seizures, this being more likely if there were focal aspects, a long seizure, positive family history, or an abnormal electroencephalogram (EEG). Alpers found patients with only one to three seizures in an entire lifetime to have electroencephalographic evidence of abnormalities and to be susceptible to alcohol, stress, or fatigue. Even after seizures have become recurrent, "cures" without medication are cited by Penfield and Erickson as occurring in 5 to 13% of cases. Wilkins found remissions in 41% of patients with infrequent seizures, and Lennox observed spontaneous remissions for one to five years in 23% and for over five years in 6% of his epileptic patients. These data are mentioned to indicate the variability of outlook for patients with single, as well as multiple, seizures.

From the Dr. W. H. Groves Latter-Day Saints Hospital.
Read before the Section on Nervous and Mental Diseases at the 107th Annual Meeting of the American Medical Association, San Francisco, June 27, 1958.

Methods and Results of Study

The Latter-Day Saints Hospital EEG Laboratory was opened in January, 1950, to serve a representative cross section of patients having a variety of neurological disorders, with a 2:1 proportion of outpatients to inpatients. For present purposes, records for the five-year period up to Jan. 1, 1955, have been reviewed. The original doctors' records have been checked as to follow-up status for three and one-half to eight and one-half years and letters sent out to patients to check on the remainder. In the five years, 48 of a total of 1,054 electroencephalograms were studied because the patient concerned had had only a single seizure. A breakdown of these cases may clarify the nature of the problem and help in planning further study and treatment.

The patients referred for electroencephalographic study after a single seizure ranged in age from 2 to 66 years, but two-thirds of them were about

equally distributed through the 30-year span from 21 to 50. It is felt that this pattern may simply reflect a greater medical nonchalance toward seizures early and late in life.

Electroencephalograms were found to show generalized abnormality in one-half, localized abnormality in one-fourth, and normal findings in one-fourth. All seizures were reported as generalized except one that was in the right arm only and one that began with unilateral jerking. A family history of seizures was present in only 12.5%.

The underlying pathological basis for the seizure was not clearly defined in over half the cases, although many of the patients had x-rays, spinal punctures, air studies, or other examinations. The remainder appeared related to trauma, encephalitis, alcohol, insulin, cerebral Hodgkin's disease, or carbon monoxide exposure. The patients with encephalitis and Hodgkin's disease died, and the disease was confirmed by autopsy. No primary brain tumors were found in this series. Of the 48 patients seen after a single seizure, 13 (27.3%) had subsequent attacks, which occurred from a few days to a few years after the patients first were seen. All of these recurrent attacks were generalized, although only half of the electroencephalograms showed generalized abnormality. Only 1 of the 13 patients had had a normal electroencephalogram, and one had a family history of seizures. Age range and distribution of the apparent causes was similar to those of the larger group. Except in the patients with fatal cases of encephalitis and Hodgkin's disease, findings on x-rays and spinal fluid or air studies were negative. Seizures were well controlled subsequently with diphenylhydantoin (Dilantin) sodium therapy when it was used consistently. In some cases, medication was later gradually decreased without further recurrence of seizures.

Management of the Patient

With this background, we can turn to the problems involved in study and management of the patient who has had a single seizure. All too frequently, this consists of a brief, incomplete, often telephoned report of the attack, followed by a general reassurance by the physician that it will not happen again.

It is of primary importance to establish from the beginning, as definitely as possible, that one is actually dealing with a seizure problem, since some harm may result from the overzealous study and treatment of hysterical or other episodes resembling seizures. The electroencephalogram is helpful, but it cannot be used alone for differentiation. Nothing can substitute for an accurate, detailed history, with an insistence at all times on an objective, eye-witness description if anyone saw any part of the attack. Particular attention is paid to contributory factors, as, for example, in alcoholism, where a somewhat different situation prevails in which primary attention to the alcohol problem may be more important.

Similarly, these cases underline the importance of additional first-level studies, including a review of the general medical history, the general physical and neurological examination, routine blood and urine studies, and any special studies suggested by these.

As for a second level of studies, such as x-ray and electroencephalogram, Doyle and others have suggested delaying until a second seizure, specifically in febrile convulsions, while Crawley, Forster, and Chao and others are less definite but imply that an examination, including x-ray and electrocardiogram, are ordinarily done after a single seizure.

Another level of studies, such as spinal fluid examination, air studies, or angiograms, should follow if specific indications appear in the course of the first two levels of study, but the latter are used less routinely where there is greater interest in the electroencephalographic evaluation. Our material is too limited in scope as yet to do more than suggest concurrence with these principles.

Even a single seizure should not be taken lightly; thus, if the first physician consulted does not feel equipped to evaluate the problem, he should enlist the assistance of someone who does have the time and interest to do so.

This careful evaluation of the patient sets the stage for appropriate subsequent management. Wherever specific pathology is disclosed, specific measures are taken, whether these are neurosurgical or they lie in treatment of concurrent medical illness. In addition, common sense advice about regularity of meals, work, and sleep or limitation of the use of alcohol or stimulants is appropriate, as with other patients with seizures, including any special considerations involved by the patient's social or occupational setting.

Medication

Next is the thorny problem of medication. In the past, most writers have waited for recurrences. More recently, Crawley and Chao have suggested treatment in selective cases but delay if the neurological and electroencephalographic findings are negative in either adults or febrile children with convulsions. In the latter group, Schmidt emphasizes the real potential hazards of seizures and urges anticonvulsive drugs in all cases, at least until the patient is 3½ or 4 years of age. The suggestions that neurological or electroencephalographic abnormality makes seizure enough more likely to warrant treatment appears sound. Farmer takes a yes-no position considering the severity of the attack, the patient's occupation, and other factors.

My experience in seeing over 27% of patients with a single seizure who have subsequent seizures suggests a somewhat more aggressive approach.

It is proposed that, after an initial major seizure, medication be suggested to the patient as the safest program for him if (1) he can and will intelligently adhere to a regular schedule and (2) he will report for periodic follow-up neurological examination and less frequent follow-up electroencephalographic study.

Outside of a hospital, there is a great difference between ordering a medicament and being sure it is taken. As in diabetes and similar conditions, education of the patient is essential to cooperation, and this is best done by the physician. Use of medication facilitates follow-up study, but the initial planning discussion is the best opportunity for reaching a mutually acceptable plan.

Some patients deny their illness or are set against any kind of medication and will stop it at the first excuse. Others are so apprehensive about their jobs or social status that they overlook advantages of medication. A frank discussion of the pros and cons of medication may include some of the ideas in the table.

Advisability of Medication After a Single Seizure

Problem	Pro	Con
Recurrence	28% in present series	Uncertainty
Medicament	Relative safety	Cost; bother; risk of interruption
"Masking" of disease	No effect on neurological or major electroencephalographic changes	Confusing if original diagnosis is doubtful
Threat of job loss	Minimized by prevention	Increased by disclosure of taking medication
Social stigma	Minimized by prevention	Established by use of medication

The risk of interruption of medication precipitating seizures can be minimized by the patient's cooperation. The risk of masking seizures by medication has been overemphasized and is minimized by careful follow-up study. In the job and social area, medication can be a two-edged sword, being protective in preventing seizures, but, potentially, putting the patient in a lesser jeopardy by permitting his need for such medication to become known. The latter can be minimized by simplification of dosage schedules to avoid his taking the medicament at school or work.

Once a medication schedule is set up, the interval management depends entirely on the patient's response and on follow-up examinations as a basis for future planning.

In the absence of other specific criteria, gradual termination of medication should be done in a fashion similar to that used with recurrent seizures. Most authorities suggest about a two-year period of freedom from seizures before this is done, with variation according to the electroencephalographic and other findings in the individual case. Should a seizure recur, medication is resumed.

Summary

The single or initial generalized seizure is a relatively frequent problem, appearing as the reason for 1 of 22 routine electroencephalographic studies at the laboratory of the Latter-Day Saints Hospital. Over 27% of the patients are known to have had subsequent seizures within a few days or a few years afterward.

Because of the relatively high risk, after careful neurological and electroencephalographic study an anticonvulsive medication program should be proposed to the patient and a mutually acceptable plan of management worked out with him to prevent some of the serious handicaps accompanying recurring seizures.

CLINICAL NOTES

REMOTE CONTROL TYPEWRITER FOR PARAPLEGICS

Alan Ziskind, M.D.
and
Richard L. Ziskind, Boston

A control panel has been designed to enable an individual who has lost the use of his extremities to operate a typewriter at a speed and accuracy comparable to that of the average nonprofessional typist. This apparatus was developed after observing patients with neuromuscular disabilities attempting to strike the ordinary typewriter keyboard with the usual available devices. It was felt that, if a device could be constructed to allow such patients to typewrite with accuracy at a normal speed, their rehabilitational goals could be more readily and rapidly achieved. Not infrequently, the written word is the chief method of communication for these patients.

Working on the principle that neck and head muscles have the greatest residual muscular control in many instances, a remote control typewriter

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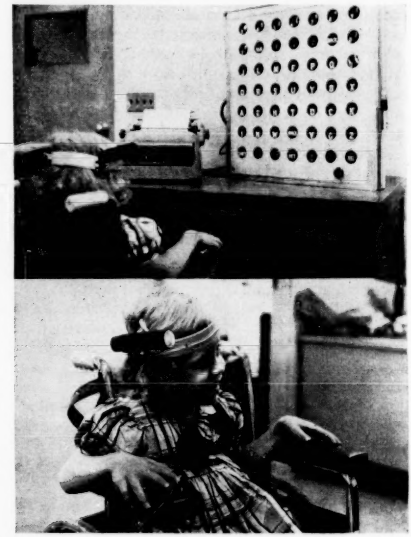
was designed to enable the patient to type with the use of this group of muscles. The photoelectric cell panel board contains a specific target area representing each key of the typewriter. This is



Top, photoelectric cell panel board connected to standard electric typewriter with solenoid box over keyboard. *Bottom*, small head lamp with parallel beam to strike letter on panel board.

coupled to a standard electric typewriter through an easily attached solenoid box placed over the typewriter keyboard (see figure). When a parallel-beam light source from a small head lamp strikes the desired target area, the letter is automatically printed. Thus, depending on the distance between light source and target board, a very small change in head position causes a relatively great excursion of the light beam on the panel. For practical purposes, a 15-degree motion of the head from a central plane in any direction is sufficient to actuate any area of the panel board.

The light beam is sufficiently small so that it cannot focus on two target areas simultaneously. Because of the problem of unintentionally sweeping over many letters in the process of selecting the desired one, a small microswitch is interposed in the circuit between the panel board and the typewriter. While learning to operate the typewriter, the individual must close this switch to complete the circuit and print a letter. Since only a small movement is necessary to operate the switch, it is easily controlled by an elbow, finger, or any area of the body where minimal motor function persists. When greater proficiency is developed, the switch is used less often since the alphabetic distribution on the board is arranged so that letter sequences form common combinations and words, and modifications are easily made for the most effective operation.

The apparatus is best suited to patients who have lost the use of their extremities through injury or spinal cord disease. There is limited applicability to the cerebral palsied or athetoid patient. Individuals with residua from poliomyelitis and those with spinal cord injuries are able to type at a rate approaching 30 words a minute. A companion device—a battery-powered court stenographic machine—is being modified to allow an individual to attend school and take lecture notes which later can be transcribed at home.

It is hoped that this device will give many of the disabled more freedom of communication, which in turn will result in improved rehabilitation and emotional adjustment.

818 Harrison Ave. (18) (Dr. Alan Ziskind).

This study was aided by a grant from the United Cerebral Palsy Foundation.

ICTERUS NEONATORUM WITHOUT ISOIMMUNIZATION.—That the premature infant can develop kernicterus in the presence of hyperbilirubinemia without evidence of isoimmunization is becoming more generally accepted. . . . The bulk of the evidence indicates that premature infants exhibit jaundice and hyperbilirubinemia more frequently and to a greater degree than is reported in full-term infants. The duration of this hyperbilirubinemia is related to fetal maturity, persisting longer in the most immature infants. Because of the variability of concentrations of bilirubin in the plasma of premature infants, and because of the multitude of factors that play a possible role in determining the ultimate concentration of bilirubin, routine exchange transfusion for elevated concentrations of bilirubin does not seem warranted. The critical level over which exchange transfusion should be done cannot be stated on the basis of any available data.—G. H. Holman, M.D., Studies on Physiologic Hyperbilirubinemia of Negro and White Premature Infants, *Pediatrics*, December, 1958.

COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report.
H. D. Kautz, M.D., *Secretary.*

The following report has been adopted by the Committee on Research.
Norman De Nosaquo, M.D., *Secretary, Committee on Research.*

EXPERIMENTATION IN MAN

Henry K. Beecher, M.D., Boston

Present Aims

Experimentation in man for scientific purposes is as old as recorded history. The need for constant examination of the procedure is equally ancient. This is required by progress in science and by the advance of ethical and moral concepts.

In the two decades just passed, two reasons have emerged which especially point up the need for a new review of the subject. First, there were the outrages of Hitler's Germany. The puzzle is how such things could have occurred in modern society. Although the philosophical problems raised by those gross actions are beyond the area surveyed in this report, they too indicate the need for a long, straight look at our current practices. Second, there is the rather newly recognized fact that some types of basic scientific advance can be made only in the presence of disease. Nature presents us with bolder experiments than we would ever dare to perform ourselves. We profit from a study of them—basic science profits. Having seen what fundamental ends can be achieved, the experimentalist is led to carry on where Nature leaves off. The purposes of human experimentation thus become deeper and more complex than ever before, and so also do the problems surrounding it, reasons enough for this study.

In most cases, the problems of human experimentation do not lend themselves to a series of rigid rules. Although one purpose of the present study is to set down views, concepts, and even "rules" that have been accepted by one group or another, this is done so that the investigator, troubled by a given problem, can find references to past thinking on this subject, and so that he can have a framework against which he can measure his problems in terms of the experiences and conclusions of others in similar situations. The breaches of ethical conduct which have come to my attention were owing to ignorance or thoughtlessness. They were not willful or unscrupulous in origin. It is hoped that the material included here will help investigators protect themselves from the errors of inexperience.

Finally, it can be said that, while human experimentation has accompanied the practice of medicine from times of antiquity, the current concept of medical research has not really been presented as such to the courts. As the courts have understood it, human experimentation has not been, nor is it now, legally recognized as a legitimate part of the physician's activities. "So far, planned and directed medical research on human beings has not been tested." [1] The universal and long-standing recognition that research is essential to the advancement of medical science and the newer recognition that some aspects of basic science cannot advance without it have led to a correct, although still extralegal, expansion of human experimentation. Curiously, such work, when well conceived and soundly conducted, is everywhere recognized as being properly within the ethical and moral concepts of our time; yet it remains outside legally. Legal inclusion will depend on an understanding of all the facets of the problem.

Brief History

The oldest world literatures contain references to experimental work with animals and man.[2] It was the practice in ancient Persia for the king to hand over condemned criminals for experimental purposes in science. Later the Ptolemies did the same in Egypt.[3] About 1,800 years ago Galen, the founder of

From the Anesthesia Laboratory, Harvard Medical School at the Massachusetts General Hospital.

experimental physiology,[4] somewhat formalized medical experimentation, but this fell under a cloud during the Dark and Middle Ages, until Vesalius in the 16th century overrode the proscription against dissection of the human body and demonstrated certain errors in Galen's concept of the circulation of the blood. Three generations later Harvey, after carrying out controlled experiments in animals and in man,[2] demonstrated the circulation of the blood. He showed, in particular, that all the blood had to pass through the heart (if his calculations of volume and velocity were correct), and thus the first idea of measurement in biological investigation bore fruit.[4] More than 100 years later, Lind, in 1747, carried out a remarkably well-controlled study and demonstrated that oranges and lemons could cure scurvy. A half-century after this, in 1798, Jenner, after controlled experiments in man, published his proof of the value of vaccination against smallpox. The world was ready for two of its greatest experimentalists, Claude Bernard and Louis Pasteur.

However, all was not smooth sailing for the eager investigator. Experimentation on other men requires a willingness to experiment upon oneself as evidence of good faith, although in a given case self-experimentation may be wholly impractical. When it is carried out, it must be done with the same safeguards that are applied to other subjects. Ivy [2] cites a number of examples to indicate that willingness without the discipline of proper controls can be misleading or devastating, or both, to the participant. In 1767, John Hunter inoculated himself with gonorrheal pus to prove that the disease was transmissible in this way. He succeeded. But from the same inoculum he also acquired syphilis and concluded that gonorrhea and syphilis were merely manifestations of the same disease. Purkinje gave himself enough digitalis to kill nine cats, so that he might study the visual changes in himself. He had cardiac pain and irregularity and vomited for a week. Hales, enthusiastic about the marvels of intravenous injection, received a half-ounce of castor oil by this route and lived to describe its remarkable effects. In 1830, Tonery, in order to convince the French Academy of the extraordinary powers of charcoal to absorb alkaloids, took with this safeguard a dose of strychnine which, without it, would have been lethal. In 1857, carbon tetrachloride was tried as an anesthetic in man; a few animal experiments would have shown it to be unsuitable. In 1894, Oliver told Schafer that he had made extracts of all the endocrine glands and had injected them into his own son. Schafer altered the experiment and was first to demonstrate the pressor effect of epinephrine in dogs and cats. Ivy concludes that "these experiments may be a tribute to the enthusiasm and bravery of these early medical scientists, but they clearly show the limitations and dangers of uncontrolled self-experimentation."

At the present time we find that able men are still in difficulties. When one shifts from a study of objective manifestation of disease to subjective effects, specifically, for example, to a quantitative study of the effects of drugs on symptoms, it becomes apparent that added controls are mandatory. Chief among these is the use of the double-unknowns approach to eliminate bias. This procedure is not possible when the experimenters are also the subjects, who, as drug experience and sophistication grows, cannot remain in ignorance of the "aura" produced by opiates, for example. The scores of studies that have been lost because of a failure to recognize and employ adequate controls have been reviewed elsewhere.[3]

Paradoxically enough, in the last century at least, those who experiment in man have been freer of attack than those who carry out animal experimentation. The ethics of human experimentation will be discussed later.

Scope

There are many good reasons for a careful consideration of the scope of human experimentation: protection of the subjects, the goals of the investigators, their research and their institutions, and the sound development of medicine. These all require a levelheaded approach to experimentation in man.

Comparatively recent developments in medicine and changes in emphasis give added weight to an examination of human experimentation at this time. Although prior experimentation in animals is absolutely necessary when possible, the crucial study of new techniques and agents must be carried out in man. The extraordinary skill of the organic chemist and the biologist, working together in identifying active agents in natural products, and the chemist's progress in creating new and promising compounds, which ultimately must be tried out in man, throw an exceptionally heavy load on the experimentalist. Man as the final test site has come into prominence only in recent decades. The current development of human biochemistry, human physiology, and human pharmacology has made it plain that man is the "animal of necessity" here. In addition, there is a new interest on the part of the truly basic scientist in human experimentation. This will be described in terms of the scientist's goals.

The investigator has many goals, and, in many aspects, they are like those of the practitioner in ultimate aim. The investigator is concerned with health and its preservation and the betterment of life as well as with the causes and consequences of disease, the mechanism and relief of its symp-

toms, correction of its signs, prevention of lasting effects of disease, and the very eradication of disease. Activities directed toward these ends involve, very often, alteration of function of the body or the mind, in health or in disease, "directly or indirectly, in individuals or groups, primarily for the advancement of . . . human welfare. Although use of a procedure or its withholding may directly benefit the person involved, its basic purpose is for elucidation and generalization." [6] When possible, investigation begins in animals but finally must be applied to man.

The goals mentioned are ancient ones. There is a new one or, more accurately, a newly recognized one. In the last decade or so, it has become increasingly clear that the study of disease in man can have a deeper meaning than once was believed to be the case. The view was widely held (and still is in some quarters) that the study of disease at the bedside level represents nothing more than applied science at best. A more thoughtful approach could long ago have led to a broader grasp of the situation: some parts of basic scientific advance (I use the term in its classical sense) are utterly dependent on disease. An abundance of examples comes to mind. Pauling's interest in "molecular disease" arose in part from work with abnormal forms of hemoglobin. Although neurophysiologists have long been interested in the biochemistry of the potassium ion, recent basic advances in knowledge of this ion have come from studies of dehydration. Knowledge of the physiology of the endocrine glands is largely indebted to the fundamental leads found in disease. The anatomy of the central nervous system has been learned, in significant part, by study of cerebrovascular accidents. Such diverse matters as the discovery and understanding of vitamins, the development of microbiology, and even the advance of genetics in study of hereditary factors in disease leave no room for doubt that truly basic science can be advanced by a study of disease processes. This awareness leads to a further extension of human experimentation. With these developments it is time to examine the many-faceted problem of experimentation in man.

Ladimer [6] has expressed it thus:

> Properly conducted experimentation [in man] by qualified scientists must therefore be considered an integral branch of biologic and medical science, but it does not thereby become customary medical practice. Nor does its essentiality and acceptance establish clearly its character or place the methods employed beyond scrutiny. The responsible professions have a duty to delineate for their own members and for a critically vigilant public the nature of medical research and the limits within which it may be properly undertaken.

These introductory remarks can be concluded with the comment that prevention of experimentation can also be an experiment, even a very dangerous one, as, for example, withholding treatment of a control group. If experimentation is to be withheld, "it should be demonstrated that the proposed experiment is more dangerous or more painful than the known [or probable] results of inaction." [7] This is an expression of an ideal, rather than a practical, possibility in most cases.

Throughout this article the aim has been to present sound background data, common-sense views, and principles of procedure rather than rules. The intricate considerations which must be brought to bear on this general subject leave room for only a few absolute statements. These are discussed in the section on Codes.

Social Necessity

In the foregoing remarks it is clearly evident that human experimentation is essential for the welfare of the race, for in medical research lies "a common benefit not obtainable by other means." [6] The development of medicine, the safeguarding of health, and some types of basic scientific advance all require human experimentation. With the recent Hitlerian acts freshly in mind, it is not surprising that responsible investigators are wary of such phrases as "for the good of society." In any case, the scientist or physician has no right "to choose martyrs for society," as Kety [8] has put it.

> It should be apparent that no stigma is attached to the performance of human experiments *per se*; disgrace and infamy can arise only through its misuse. The moral obligation of performing all human experiments, with due regard to the sensibility, welfare, and safety of the subject, must not be violated. As phrased by Claude Bernard in 1856, "Christian morals forbid only one thing, doing ill to one's neighbor." So, among experiments that may be tried on man, those that can only do harm are forbidden, those that are harmless are permissible, and those that may do good are obligatory.[9]

Unfortunately, decision is usually not so simple as this sounds; choice often lies among various shades of gray, not between black and white. The social necessity for experimentation in man operates, of course, only when the desired ends cannot be obtained in other ways, as through experimentation in animals.

Subject

Observations on the choice of a subject can be set down as follows:

1. It is often not possible to directly transfer observations made in normal individuals to the sick. The complexities here are so great that only one or two suggestive examples can be mentioned: (*a*) It is exceptionally difficult, if not impossible, to reproduce usefully in normal subjects symptoms which ordinarily arise in disease. Take, as an example, pain. Beecher [5] has compiled evidence which supports this view, in that 15 groups of investigators attempted but failed to show a dependable

relationship in man between pain threshold and the action of analgesic agents, notwithstanding scores of papers to the contrary. (*b*) There is no assurance that the high incidence of nausea in normal individuals after administration of morphine holds true for those who are in pain. Incidentally, this points to a problem not yet satisfactorily solved, that is, how to secure information on the side-effects of therapeutic agents when these side-effects may be similar to those present at times in the disease state studied.

2. Individuals who may die suddenly or who seem to be in imminent danger of death should not, under ordinary circumstances, be chosen as subjects for experimentation, however harmless the planned procedure may be. If death occurs during such an experiment, it could cast a shadow over a potentially valuable agent or useful technique, not to mention placing the investigator in a most unhappy predicament, where, although innocent, he may appear guilty.

3. It is usually unwise to study a therapeutic procedure in an individual who has also a disease unrelated to the expected therapeutic effects.

4. Lay subjects, sick or well, are not likely to understand the full implications of complicated procedures even after careful explanation.

To obtain the consent of the patient to a proposed investigation is not in itself enough. Owing to the special relationship of trust which exists between a patient and his doctor, most patients will consent to any proposal that is made. Further, the considerations involved are nearly always so technical as to prevent their being adequately understood by one who is not himself an expert. It must, therefore, be frankly recognized that, for practical purposes, an inescapable responsibility for determining what investigations are, or are not, undertaken on a particular patient will rest with the doctor concerned. Nearly always his judgment will be accepted by the patient as decisive.[10]

Or, as Guttentag [11] has put it, "one has only to think of present-day specialization in medicine in order to realize that the patient is frequently not able to grasp all the implications of a certain procedure so far as his health is concerned."

To some, this complexity leads to a strong admonition concerning voluntary work. At one time, Pfeiffer [12] held the view that one should "never use anyone except a volunteer who is at least at the level of a graduate student and who has investigated for himself the nature and possible dangers of the drug or procedure involved." Many investigators would not agree with this last view. For some types of investigation, especially when subjective factors are involved, it is essential to have subjects who know nothing about the expected results and have no vested interest in the outcome. Certainly Pfeiffer's early requirement for an informed subject cannot be complied with in the case of the diseased subject. Such difficulties, however, emphasize the increased responsibility of the investigator when the subject cannot truly understand the full implication of the study contemplated. This view is set down in some detail for comparison with this idealistic, yet thoughtful and practical, investigator's current view. Pfeiffer [13] states his present view: "My quotation from 1951 must certainly be modified as of this date since we are using prisoners at the Atlanta Penitentiary who are not graduate students! We do screen our prisoners for psychiatric difficulties by having them complete a Rorschach examination, IQ assay, and MMPI tests. We also go over their psychiatric history very carefully. My statement of 1951 represents the ideal situation rather than the practical situation."

Volunteer

Information Given.—The information given to or obtained by the volunteer subject may vary widely from none at all, when innocuous procedures are undertaken in the study of subjective responses, to full discussion whenever any risk is involved. These matters have been referred to in the preceding section.

Laboratory Personnel and Medical Students.—Laboratory personnel and medical students are often considered legitimate game by the eager but impoverished investigator, and certainly tradition has accepted their use. In my opinion, at least, there are two reasons why such groups are usually not a good choice: 1. In a sense, these are captive groups, not so seriously so as prisoners of war perhaps, but nonetheless available for certain kinds of subtle coercion. A volunteer should be just that, not one who may be subject to fear of the consequences if he does not cooperate. The more domineering the investigator, and thus the more valid the point made, the more likely is this possibility to be disclaimed. Denied or not, the situation does exist; it is better to avoid it. 2. In quantitative studies of subjective responses over many years, it has become clear to me that, in this field at least, subjects must not be in communication with each other, for, if they are, certain false "syndromes" are "established," through conditioning presumably. Lack of space precludes citing some startling examples of this. The hazard to sound conclusion of such action is nowhere more amusingly evident than in the reports of some of those who have studied the effects of psychotomimetic drugs in their own personnel.

Mackintosh,[14] however, has expressed a sound and considerate point of view concerning the use of laboratory personnel:

On the difficult question of laboratory personnel, we had certain decisions to make in the London School of Hygiene. In the study of malarial parasites "resting" in the human liver we had offers from a skilled technician to submit himself to infection and then to have a small liver section taken. In this case the technician was a senior man who was fully aware of the risks involved. His offer was gratefully accepted, but at the same time a regulation was passed that in the

future no human experiment should be allowed without a full report being made in advance to the School Council (which is the professional body) and to the Board of Management, which has a considerable representation of scientists, and also lay members. The crux of the decision was whether the volunteer had the training and skill to appreciate the whole situation, although not necessarily the details of the procedure. It was evident that there might be subjective matters of study which the volunteer ought not to know beforehand, so as to avoid vitiating the experiment. The additional point of the decision was to make sure that the volunteer gave his consent freely, or, better still, offered his service in writing. In such cases no fee or reward, apart from any out-of-pocket expenses, should be offered.

Lasagna and von Felsinger [15] have discussed the "ample reason(s) for wariness in making generalizations regarding drug effects from a study, no matter how careful, of any *single* group of individuals, be they sick or healthy, volunteer or non-volunteer."

Civil Prisoners.—The major scientific contributions which have come directly from utilization of civil prisoners who have volunteered for such endeavors offer at least a pragmatic justification for the practice. Possibilities for direct or indirect coercion, flagrant or subtle, are so great that use of these individuals must be considerate indeed to be sure that there has been no coercion. The practice has a rather long history. Included as civil "prisoners" are the inmates of orphanages [16] and asylums for the insane [17] as well as prisoners in jail.[18] During World War II both federal and state prisoners made important contributions to malaria studies, the use of blood plasma, plasma fractions, and plasma substitutes, and trials of various new drugs. In most prisons more volunteers were available than were needed.[2]

The advisory committee [18d] appointed by Governor Green, of Illinois, had this to say:

Since one of the purposes of the parole system is reformative, the reformative value of serving as a subject in a medical experiment should be considered. Serving as a subject in a medical experiment is obviously an act of good conduct, is frequently unpleasant and occasionally hazardous and demonstrates a type of social consciousness of high order when performed primarily as a service to society. The extent to which the service of a prisoner in an experiment is motivated by good social consciousness on the one hand and by the desire for a reduction of sentence in prison on the other is a matter for consideration in the case of each prisoner. Regardless of a prisoner's motives for volunteering for an experiment, a habitual criminal or a prisoner who has committed a notorious or heinous crime should not be considered an acceptable volunteer for a medical experiment.

The rewards for prisoner volunteer service vary all the way from gifts of tobacco [18e] to a full pardon.[18b] Cautioning against excessive rewards, the Green committee said:

The most important requirement for the ethical use of human beings as subjects in medical experiments is that they be volunteers. Volunteering exists when a person is able to say "yes" or "no" without fear of being punished or of being deprived of privileges due him in the ordinary course of events.

A reduction of sentence in prison, if excessive or drastic, can amount to undue influence. If the sole motive of the prisoner is to contribute to human welfare, any reduction in sentence would be a reward. If the sole motive of the prisoner is to obtain a reduction in sentence, an excessive reduction of sentence which would exercise undue influence in obtaining the consent of prisoners to serve as subjects would be inconsistent with the principle of voluntary participation.

The committee added the somewhat unrealistic comment: "Obviously no one may make representations to a prisoner concerning the extent and types of reward which may accrue as a result of his service as a subject in a medical experiment." In all examples I have seen, the terms were explicitly stated beforehand and were always lived up to after the fact.

Military Prisoners.—It is never permissible to use prisoners of war for experimentation. This is the sound policy of the Department of Defense.

Volunteer Corps

Hogben and Sim [19] have this to say:

If we approach the problem [of human experimentation] against a background in which the major advances of medicine occurred in the social setting of pestilences, practical difficulties of enlisting volunteers without violence to ethical standards are easy to exaggerate; but a wholesome regard for the sanctity of life becomes increasingly less relevant to a statement of the priorities of medicine in western communities with a life-expectation well above 60 years at birth. There is indeed an ever more pressing need for knowledge about many once-thought *minor* evils. We cannot effectively tackle them by group methods; but we might well do so with the help of individuals now willing to risk life or limb on the speedway or in the ascent of Mount Everest, if we could institutionalize a not uncommon appetite for adventure consistent with acceptable moral standards. It is not beyond the reach of social engineering to create a new corps of civil defence with that end in view. The voluntary response to the appeal for blood donors disposes of doubts about the feasibility of such an undertaking, if sponsored by an adequately accredited organization.

We have in the United States the beginnings of such a corps in the group of conscientious objectors to military service who volunteer, and also in the Mennonite group of young adults who volunteer as subjects for scientific studies.

Investigator

Characteristics and Qualifications.—The physician and the investigator are different in their procedures, in their aims, and in their immediate ends. To paraphrase Ladimer,[6] the physician accepts patients and is mainly concerned with their welfare; the investigator selects subjects (problems as well as individuals) and, while responsive to the patient's interest, is bent on solving the scientific problem. But "one irresponsible investigator can do great harm to medical science." [20]

All the so-called codes as guides to human experimentation emphasize the necessity that the experimenter be well trained and adequate as a scientist

to undertake the study proposed. Medical research, when it involves treatment or any physical procedures beyond the simplest type, requires that the investigator or his close associate be a qualified physician. No other profession gives such prerogatives, and no other profession, probably, presents such a generally high level of unselfishness and compassion. Of these two qualities, unselfishness is the more important for subject and project alike. Imagination, objectivity, and the power to generalize soundly are all essential.

Responsibilities and Safeguards.—Claude Bernard [21] stated the responsibilities of the investigator as follows:

> As far as direct applicability to medical practice is concerned, it is quite certain that experiments made on man are always the most conclusive. No one has ever denied it. . . . First, have we a right to perform experiments and vivisections on man? Physicians make therapeutic experiments daily on their patients, and surgeons perform vivisections daily on their subjects. Experiments, then, may be performed on man, but within what limits? It is our duty and our right to perform an experiment on man whenever it can save his life, cure him, or gain him some personal benefit. The principle of medical and surgical morality, therefore, consists in never performing on man an experiment which might be harmful to him to any extent, even though the result might be highly advantageous to science, i. e., to the health of others. But performing experiments and operations exclusively from the point of view of the patient's own advantage does not prevent their turning out profitably to science.

Bernard's view cannot soundly be construed as ruling out risk when there is hope of gain; both must be weighed.

In patently nonhazardous experimentation, there is no necessity for the investigator to subject himself first to the experimental procedures. However, whenever doubt exists as to safety, it is advisable for the investigator first to subject himself to the possible hazards involved.

When it is not known whether a given treatment is likely to be effective, the investigator is entitled to withhold it if new and more promising therapy waits trial. However, he is not entitled to withhold therapy when its effectiveness is assured, except with the consent of the patient. Green states it thus: "where the value of a treatment, new or old, is doubtful, there may be a higher moral obligation to test it critically than to continue to prescribe it year-in-year-out with the support merely of custom or wishful thinking." [22] McCance has said: "the medical profession has a responsibility not only for the cure of the sick and for the prevention of disease but for the advancement of knowledge upon which both depend. This . . . responsibility can only be met by investigation and experiment." [20]

Although many differences exist between the practice of medicine and human experimentation, there are, nonetheless, certain parallels that can usefully be drawn in examining one's position of responsibility. In questions of malpractice a legitimate point is whether the actions of the physician were in accordance with generally accepted standards in the given case. So too the same question can be appropriately raised concerning experimentation.

> In research, standards must relate to how the investigator proceeded and how he checked himself. The means by which research of high quality has been managed and the safeguards employed to protect the subject can be generalized into a set of precepts similar to that governing malpractice, to serve as a guide. Thus, willful or negligent deviation, resulting in injury, would constitute a basis for liability. On the other hand, observance of all known precautions, even in the event of an untoward result, would protect the honest, qualified investigator. Neither he nor the physician is a guarantor of success, but each has a responsibility to his own law and credo.[6]

The responsibilities devolving on those who undertake experimentation in man are so great that, whenever even remote hazard is a possibility, group decision supported by a proper consultative body should be employed.[7] Self-experimentation "without such collaboration and consultation seems as indefensible as similar experimentation on another individual." [7] "At the Clinical Center of the National Institutes of Health, for instance, projects involving deviation from accepted medical practice or unusual hazard are presented in writing to a Clinical Research Committee. Consent is obtained from subjects and final approval from the Center's Medical Board and the Director of the National Institutes of Health." [6] The British Medical Research Council has said:

> In any particular case—so specialized has medical knowledge become—only a small group of experienced investigators, who have devoted themselves to this branch of medicine, are likely to be competent to pass an opinion on the advisability of undertaking any particular investigation. But in every branch of medicine such a group of investigators exists. It is upon them, and the specialized scientific societies to which they belong, that the medical profession must mainly rely for the creation of the body of precedents and the climate of opinion which shall guide investigators in clinical research . . . it is incumbent upon the medical scientific societies to accept this responsibility and, by encouraging critical discussion on the communications presented to them, help to resolve doubts and to form a body of opinion of what is necessary, desirable and justifiable to guide investigators in their field.[10]

Wiggers [9] has expressed a similar view.

The Department of Hospitals, City of New York, issued an order in which is stated: "#1 That proposed clinical or laboratory investigations in any hospital or institution of the Department, whether or not under the auspices of affiliated medical schools, be submitted for review and approval by the Executive Committee of the Medical Board of the hospital concerned.

"#2 That unless it is specifically designed to benefit the patient involved—no research using a patient as a subject is permitted in any hospital or institution of the Department." [23]

Relationship Between Subject and Investigator

This relationship very often is identical with the patient-physician relationship and will be considered from that viewpoint. There is good reason why this facet of the human experimentation problem should be considered. Whenever the physician tries out a new drug or a new technique—not necessarily new in any absolute sense, perhaps only new for his particular patient—he is experimenting in his effort to relieve or cure the individual involved.[24] It could often be shown to be wrong to withhold such methods of trial. Such "experimentation" is, in principle, relatively uncomplicated. Great complications arise, however, when the experimentation on one patient is not expected to benefit the immediate patient but is for the good of patients in general. Recent increase in this type of experimentation requires consideration, for such a matter involves the most basic elements in the patient-physician relationship as well as the attitude toward life and its responsibilities of both the patient and the physician. As Guttentag [11] puts it, "not all experiments performed on men will ever be of value to these particular men. And it is with these breathing men that we are concerned as physicians."

Only physicians can legally take the responsibility for medical experimentation on man. In any case, no one else is so well equipped to carry out work "to confirm or disprove a biological generalization with regard to man . . . [than] the profession that is trained more completely than any other in comprehending the somatic and psychological aspects of human life, be it healthy or diseased." In addition to this reason there is another. As Guttentag [11] points out, it is related to the original patient-physician relationship: "Here *both* the healthy and the sick persons are . . . fellow-companions, partners to conquer a common enemy." Guttentag has called it " 'mutual obligations of equals' or to use Weizsaecker's term, it is 'solidarity.' Objective experimentation to confirm or disprove some doubtful or suggested biological generalization is foreign to this relationship." He considers the physician-experimenter and the physician-friend as two distinct aspects of the doctor.

Against the background of the two roles played by the physician, Guttentag [11] considers three currently evolving developments. First, there is the use of force as exercised in Hitler's Germany. It seems unlikely that this will be of importance in this country, except for extremely rare local abuses, for the overwhelming majority of physician-experimenters, if not thoroughly aware of the nature of the original patient-physician relationship, are so deeply rooted in the democratic spirit that they agree, and will continue to agree, that the use of force is not justified on a single person, even if millions of other lives could be saved by such an act. They realize that as an amoral act from the standpoint of democratic brotherhood, it might create millions of amoral sequels, and that the moral history of mankind is more important than the scientific.

Second, the use of the "hopelessly incurable" as experimental subjects has developed recently. I have already stated the reasons for my deep conviction that those who are in imminent danger of death should not be subjected to experimentation, except as part of the therapeutic effort for the benefit of the subject himself. Occasionally, reports are found wherein use of the "hopelessly incurable" seems to justify dangerous experimentation. The error in this appears evident. It is not the physician's prerogative to make or to profit from such dubious judgments. The use of such subjects is meant to be noble in the democratic spirit, yet it unconsciously challenges this spirit more subtly but no less than the use of force, because it violates the concept of equality or brotherhood in violating the principle of the original patient-physician relationship. From the experimenter's point of view, the description "hopelessly incurable" is not germane to his purpose. The designation is inadequate, because it does not specify the time element—hopeless within hours, days, months, years? And if months or years are concerned, do all experts agree on the status of their respective sciences and deny the possibility of discovering effective agents within such a period? The term is also unnecessary. . . . From the standpoint of the physician-friend, the assertion is not germane to his purpose, either. To him it is an expression of detachment between physician and patient, the announcement of a scale of partnership vs. domination quite contrary to its original spirit. As a matter of fact, it creates the paradox that the healthier the patient, the more he should be the concern of his physician; the sicker, the less.[11]

Third, "increased technicalities of many problems and procedures" have arisen. To Guttentag [11] this suggests that for the protection of the subject the physician-friend and the physician-experimenter should be two persons, lest selfishness decide the issue. The physician-friend would play the part of attorney for the defense, whereas the physician-experimenter would be the prosecuting attorney. Practically, the physician-friend and the physician-experimenter must sometimes, and often will, be the same person. Nevertheless, it is necessary that the two attitudes be recognized and pondered.

Justification for Human Trial

The importance of the project undertaken must be commensurate with the risk involved. The insurance of this is a cardinal responsibility of all who undertake experimentation in man. However, there is still a vast area where judgment—one hopes sound judgment—must operate. Only the fanatic denies that animal experimentation must precede human experimentation. As Sir Geoffrey Jefferson [25] put it, "Man is too rare, too expensive, altogether too valuable an animal" to be first used in the study of technical procedures or trial of even therapeutic agents. There are, at the same time, species differences. Ultimately, the definitive test must be

made in man. Certain types of experimentation are impossible in animals and must be done in man, as discussed in the following section.

Types of Human Experimentation

These classifications can be considered from various points of view. For example, one scheme is based on the patient's role: (1) "passive," in which human tissues or products are examined, as by the pathologist or biochemist; (2) "late active," in which studies are applied to the patient only after prior investigation on animals; and (3) "initial active," in which work must be undertaken exclusively on man.[7] Another classification is based on the purpose of the research; that is, whether it is designed to be of value to the immediate patient under study or to patients in general. Still other categories of consideration are reasonable; for example, whether the investigation is to advance basic science or whether it falls into the realm of applied science.

The reviewer must confess to scant interest in such schemes. There are, however, several points that should be made, points which cut across various classifications.

1. Prior controlled experimentation in animals is absolutely essential whenever this is advantageous, and this is almost always, in one way or another, the case. Even when primary drug effects cannot profitably be studied in animals, possible toxic effects can and should be.

2. In certain circumstances, experimentation in animals is impossible or useless. For example, mental disease and its prodromal states must be studied in man. Studies of subjective responses, symptoms, require human subjects, although useful inferences can be drawn in some cases from animal work, for example, studies of the effect of analgesic agents on animal withdrawal reflexes presumably produced by pain. Since certain syndromes and diseases do not occur in animals, obviously they must be studied in man.

3. Although the investigator should be willing to serve as a subject in any project having even remote possibilities of hazard (as evidence of his good faith), self-experimentation is an unwise performance whenever judgment can enter into the conclusions drawn.

4. Any classification of human experimentation as "for the good of society" is to be viewed with distaste, even alarm. Undoubtedly all sound work has this as its ultimate aim, but such high-flown expressions are not necessary and have been used within recent memory as cover for outrageous ends.

Permissible vs. Nonpermissible Human Experimentation

Very often decision lies between two shades of gray.[26] When hazard is involved, or may be present, group decision by one's peers becomes important. Ivy [2] has presented some telling examples of rash or foolish experimentation. On top of all his other problems, the harassed investigator recognizes that sometimes to prevent an experiment may of itself be also an experiment, even a dangerous one.

Pope Pius XII [27] expressed the stand of the Roman Catholic Church thus:

> In the domain of . . . science it is an obvious law that the application of new methods to living men must be preceded by research on cadavers or the model of study and experimentation on animals. Sometimes, however, this procedure is found to be impossible, insufficient or not feasible from a practical point of view. In this case, medical research will try to work on its immediate object, the living man, in the interests of science, in the interests of the patient and in the interests of the community. Such a procedure is not to be rejected without further consideration. But you must stop at the limits laid down by the moral principles We have explained.

Propriety in Publication

When reports on human experimentation are prepared for publication,

> It cannot be assumed that it will be evident to every reader that the investigations being described were unobjectionable. Unless such is made unmistakably clear misconceptions can arise. In this connection a special responsibility devolves upon the editors, and editorial boards, of scientific journals. . . . It is desirable that editors and editorial boards, before accepting any communication, should not only satisfy themselves that the appropriate requirements have been fulfilled, but may properly insist that the reader is left in no doubt that such is indeed the case.[10]

There have been instances in which certain details and complications have been deleted from published reports to avoid unfavorable criticism. It seems unlikely that such abuses are common, but when they occur, it is probable that the study should not have been carried out in the first place. The failure to report serious complications in a final report is inexcusable.

Ethical and Moral Aspects

The physician, with his 2,500-year-old traditions and his constant preoccupation with problems of life and death, has understandably had a long concern with ethical matters. The first codification of such matters in the United States occurred in 1848,[28] when the American Medical Association patterned its statement on Sir Thomas Percival's "Medical Ethics" of 1803. The principal categories concerned the relationship of the physician to society, to his patient, and to his colleagues.

There have been a good many controversies involving medical ethics in the past 20 years. Fitts and Fitts [29] have suggested as various causes for this the splintering of medical knowledge into numerous specialties, leading as it does to group practice; the spread of insurance schemes, with intrusion of a third party between the physician and his patient; and finally "the radical treatment of serious disease, which appears, when first applied,

to verge dangerously upon human experimentation." The implication of this last comment, i. e., the radical treatment of disease, however close to the legal stand it may be, is possibly at variance with present widespread humanitarian concepts.

Changes in ethical considerations may be slow, but they do occur and are illustrated in correspondence to the Royal Society in England. In 1756, Sir Hans Sloane described how,

> The princess Anne, now princess royal of Orange, falling ill of the small-pox in such a dangerous way that I very much feared her life, the late Queen Caroline, when princess of Wales, to secure her other children, and for the common good, begged the lives of six condemned criminals, who had not had the small-pox, in order to try the experiment of inoculation upon them. But Mr. Maitland, who had inoculated at Constantinople, declining for some reasons to perform the operation. . . . [but later he was persuaded and] undertook the operation, which succeeded in all but one, who had the matter of the small-pox put up her nose, which produced no distemper, but gave great uneasiness to the poor woman. . . . To make a further tryal, the late Queen Caroline procured half a dozen of the charity-children belonging to St. James' parish, who were inoculated, and all of them, except one (who had had the small-pox before, tho' she pretended not, for the sake of the reward) went thro' it with the symptoms of a favourable kind of that distemper.

The very fact that such a performance on the part of the present royal family of Great Britain would be unthinkable emphasizes the change.

This ethical change is further exemplified in recent correspondence to *Lancet*, in which the discussion, even though pros and cons are presented, indicates a lively conscience. In the letter which started this correspondence, Fisher [30] had this to say:

> It is a matter for regret that the use of normal children (or children suffering from some irrelevant disease) as controls in clinical research appears to be increasing.
>
> No medical procedure involving the slightest risk or accompanied by the slightest physical or mental pain may be inflicted on a child for experimental purposes unless there is a reasonable chance, or at least a hope, that the child may benefit thereby.
>
> If this is true—and I hope that there are few doctors in this country who would disagree—then it must surely be difficult to justify the use of two hydrocephalic infants reported in the paper by Dr. Doxiadis and his colleagues, and the use of a normal control by Dr. Bickel and his colleagues.
>
> It may be, of course, that there were some good reasons for the use of these children which have not been made clear.

Holt [31] replied for one group of authors:

> It is quite reasonable that Dr. Fisher should raise the question of the use of normal children or children suffering from some irrelevant disease as controls in clinical research. There are extreme opinions on both sides, but I feel most of us adopt a policy between the two—somewhere in the grey between the rather theoretical white and black. My own working policy, which differs slightly from that expounded by Dr. Fisher in the second paragraph of his letter, is that no procedure should be carried out involving risk or discomfort without a reasonable chance of benefit to that child *or other children;* and this principle was followed throughout our work. The crux of the matter is contained in the last sentence of Dr. Fisher's letter—we owe it to ourselves to explain our actions. Surely we all weigh these matters most carefully in our own consciences.

Further comment was made by Bickel and Gerrard: [32] "We are grateful to Dr. Fisher for raising a problem of which we are fully conscious in our daily work. Nevertheless, errors of metabolism constituting the underlying cause of many diseases cannot be understood or properly treated without knowledge of normal physiology."

Leys [33] commented on the previous correspondence:

> The privileged position which doctors hold in society depends entirely on the trust which people have in the purity of their motives. This is stated explicitly in the international code adopted by the World Medical Association in 1949: "Under no circumstances is a doctor permitted to do anything which would weaken the physical or mental resistance of a human being except from strictly therapeutic or prophylactic indications imposed in the interests of the patient." There is no justification here for risking an injury to an individual for the possible benefit to other people, as enunciated by Dr. Holt as his guiding principle. Such a rule would open the door wide to perversions of practice, even such as were inflicted by Nazi doctors on concentration-camp prisoners. The magnitude and crudity of their "experiments" must not be allowed to blunt sensitivity to breaches of the medical ethic made on a smaller scale and with greater plausibility. Of this nature are experiments performed upon condemned criminals, with or without the victim's consent, upon conscientious objectors to military service, upon persons with chronic mental illness or deficiency or incurable disease of any kind, and all procedures, whether therapeutic in intent or not, which are not designed with the sole intention of improving the lot of the individual upon whom they are performed. Only one exception can be allowed—i. e., when the experimental subject is an adult whose judgment is not impaired and who freely gives his consent. No child must ever be the subject of such an experiment.
>
> It is clear that the assumption by doctors of scientific methods and techniques calls for critical examination of the uses to which these methods are put. The scientific material of the clinical research-worker is human life.
>
> I should like to see a resumption of the practice by which all doctors upon qualification were required to make a declaration of adherence to the medical ethic. There is need for a revised, more simple form of the Hippocratic oath, relevant to the circumstances of the 20th century. For some time the ethics subcommittee of the Medical Association for Prevention of War has been occupied with such a revision, and I give, for the sake of discussion, the tentative and interim results of this attempt.

Items (2) and (4) of the revised oath are pertinent to the present discussion:

> (2) To direct all my work to the preservation of life and the relief of suffering, and under no circumstances whatever to use my medical knowledge to harm any person, nor take part in any experiment involving risk of injury, without assuring myself of the understanding and freely given consent of an adult subject, nor without consulting my colleagues upon the value and necessity for such an experiment.
>
> (4) To communicate freely to all doctors any discoveries which I believe myself to have made concerning the nature, cure, or prevention of disease.

Ethical and moral implications and problems surround every facet of experimentation in man. This has been evident in each of the preceding sections of this report. The central conclusion is that it is unethical and immoral to carry out potentially dangerous experiments without the subject's knowledge and permission. Every act of a physician designed soundly to relieve or cure a given patient is experimentation of an easily justifiable kind. The patient's placement of himself in the physician's hands is evidence of consent. The problem becomes a knotty one when the acts of the physician are directed not toward benefit of the patient present but toward patients in general. Such action requires the explicit consent of the informed patient. It also requires more than this—it requires profound thought and consideration on the part of the physician, for the complexities of medicine are, in some cases, so great that it is not reasonable to expect that the patient can be adequately informed as to the full implications of what his consent means. His trust in the physician may lead him too easily to say yes.[34] Although there is no excuse for failure to do one's best to present an accurately informative picture to the subject, it is an injunction to the experimenter himself to cultivate a deep sense of his own responsibility in such a case.

"The patient, however humble and however ill, in whatever degree derelict and forlorn, has sacred rights which the physician must always put ahead of his burning curiosity." [3] The situation is a safer one, as Guttentag points out, when the "physician-friend" who looks after the patient's illness and welfare in general is not the same person as the "physician-experimenter."

"The ethical principles involved in the use of the mentally incompetent are the same as for mentally competent persons. The only difference involves the matter of consent. Since mental cases are likened to children in an ethical and legal sense, the consent of the guardian is required." [2]

The ethics and practice of placebo therapy have been reviewed and discussed in considerable detail by Leslie [35] who concluded, "The proper use of the placebo requires, in addition to broad medical knowledge, a depth of human understanding not requisite to the purely materialistic approach to medicine."

In a speech delivered on Sept. 14, 1952, Pope Pius XII [27] discussed the moral limits of medical research and treatment and, in particular, the interests of science as justification for research and the use of new methods. If a procedure "cannot be used without injuring the rights of others or without violating some moral rule of absolute value . . . morally the method is not admissible," even though knowledge might be increased by its use. The reason for this is that, just as science is not the highest good, so also the desire for scientific growth cannot override certain moral values. "Science itself, therefore, as well as its research and acquisition, must be inserted in the order of values."

Further discussion by the Pope concerned the interests of the patient as justification of new medical methods of research and treatment. The physician's rights or power over the patient or subject are only those given by the subject, bearing in mind that "the patient cannot confer rights he does not possess." According to this philosophy, "The patient, then, has no right to involve his physical or psychic integrity in medical experiments or research when they entail serious destruction, mutilation, wounds or perils."

A third interest is the *bonum commune* or common good. The two interests already discussed, that of science and that of the patient, are closely allied to the general interest. This leads to the question, "Can public authority, on which rests responsibility for the common good, give the doctor the power to experiment on the individual in the interests of science and the community in order to discover and try out new methods and procedures?" The answer is obviously "no,"[27] for the individual must not be subordinated to the community; the community exists for the man.

Legal Considerations

The legal considerations surrounding human experimentation have been exhaustively reviewed and documented by Ladimer.[36] Appropriate to the present report is a statement of the basic assumptions and general principles involved. In addition to this, attention will be called to some surprising lacks of legal precedent in this field.

The practice of medicine has been described over some thousands of years in recorded history, and during this vast period it has been hedged about with innumerable oaths, precedents, customs, rules, orders, and laws for the protection of the patient. Human experimentation is as ancient as the practice of medicine; yet, remarkably enough, no specified legal precedents have been set down to protect the subject or the investigator. At the same time there is an abundance of precedent to indicate that, however able, skillful, conscientious, well trained, and generally well qualified the investigator is, he experiments on man to his peril. The first malpractice suit involving alleged experimentation occurred in 1767, *Slater* v. *Baker*. It "established the rule that experimentation was at the physician's peril," [36a] although the court commented at the time on the surgeon's good character and repute.

As Ladimer [36a] has put it, the position taken by strict legal writers and jurists who have summarized the issue's present position is as follows: In treating the patient "there must be no experimentation . . .

we find that legal encyclopedias have unwaveringly set forth that while it is the duty of the physician or surgeon to keep up with advancements in his profession, it is also his duty not to try to forge ahead of it by trying experiments." The doctrine is: "The physician experiments at his peril." Many similar examples could be given. In this seemingly harsh stand "the law" seems to close its eyes to reality, for, as every able physician knows, the adequate practice of medicine involves continual experimentation. No two patients respond precisely alike to any therapeutic procedure. Even in ordinary practice the able physician experiments until his treatment is successful or the patient dies.

The precedent and interpretations just mentioned have to do with the comparatively simple situation of experimentation designed to benefit the immediate patient. The important but much more difficult situation remains, and is scarcely mentioned in legal discussion, in which the research is not designed to benefit the immediate patient but rather patients in general.

To a layman like myself, this is an instance in which the law and its interpretation are far removed from actual practices and from current, universally accepted ethical and moral concepts of Western civilization.[36a] These concepts can be summarized as follows: 1. Progress in the medical sciences depends upon research. 2. Much of this research requires human experimentation. 3. Human experimentation is necessary and proper. 4. It is not considered just that a man be placed in jeopardy or penalized for helping his brother.

The need for a redefinition of human experimentation becomes apparent, because many court rulings equate experimentation with "rash action" and "ignorant and unskillful departure from approved methods." The low esteem of the court for such experimentation is expressed in such phrases as "rash or experimental methods," "mere experiment," or "reckless experiment." By no means could all the acts so castigated be labeled as foolish, nor were they always the work of incompetents. The remarks quoted, "quite typical in cases of this kind reveal[s] the association in the judicial mind between experimentation and professional disregard or negligence. Needless to say, this represents either a complete misconception of scientific experimentation or the singular use of the term so that it partakes of reckless behavior or quackery. . . . The term 'experimentation' has been used loosely by the courts," so says Doctor of Jurisprudence Ladimer, as I would scarcely dare to do. He points out that the precedents, the cases of record, have "dealt not with major problems baffling to medicine and science on which basic research or applied clinical study was required, but with questions which confront the regular practitioner."

In his superb review Ladimer [36a] has said:

> The term "experimentation" must be considered objectively (preferably discarded if it retains the connotation of improper medical practice) so that it is recognizable as a legitimate scientific endeavor which can be advanced by the recognized research scientist. The legal issue would then become not experimentation versus accepted practice of the art of medicine but an evaluation of the plan and conduct of research in relation to specific fact situations, that is, whether the research was conducted with due regard to the interests of the subject. The law has a duty to comprehend the scope and elements of diverse human activity and their places in society if it is to assist in making individual judgments and setting or recognizing general values. . . . Essentially, medical research on human beings consists in experimentation, that is, deliberately inducing or altering body or mental functions, directly or indirectly, in individuals or in groups primarily for the advancement of health, science and human welfare.

Continuing, Ladimer [36a] has maintained that medical research

> is significantly different from medical practice in such respects as purpose and attitudes, scientific problem or medical hypothesis, study design or treatment, relative obligations of physician-researcher and patient-subject and general environment including scientific staff, facilities and types of clinical material selected. . . . The conduct of medical practice, generally conceived to be diagnosis, treatment and care, is governed by state statute and supporting administrative licensing and regulatory bodies. Medical research on human subjects, except as it is an inherent but not predominant incident of such practice, would appear to be outside the scope of [medical practice]. . . . There is no existing broad police power statute for control of human research although it is, by its nature, subject to the general police power.

Human research "today warrants [legal] recognition as a separate endeavor affected with a public interest as significant as medical practice itself."

Codes

As already mentioned, it is not my view that many rules can be laid down to govern experimentation in man. In most cases, these are more likely to do harm than good. Rules are not going to curb the unscrupulous. Such abuses as have occurred are usually due to ignorance and inexperience. The most effective protection for all concerned depends upon a recognition and an understanding of the various aspects of the problem. Eventually, the broad gap between the law of the land and its interpretation, on the one hand, and scientifically, ethically, and morally sanctioned experimentation in man, on the other hand, must be narrowed, if not closed. This legal development can be helpful and directed toward progress or can be harmfully restrictive. Which it shall be will be determined by the breadth of understanding expended on this complex subject.

Since only physicians can accept the responsibility for human experimentation, beyond the simplest procedures, the oath of Hippocrates has been a

basic guide. The physician agrees to work to the best of his ability for the good of his patients and to "abstain from whatever is deleterious and mischievous." As Claude Bernard [21] put it a century ago: In the field of experimentation "Christian morals forbid only one thing, doing ill to one's neighbor." In terms of principle, these elevated sentiments possibly say all that is necessary. The writer, in common with many other investigators, has sought a practical spelling-out of the principle involved. Various attempts to do this will now be described, using as the basic framework for discussion the 10 points developed at the Nuremberg Military Tribunals.[37]

Nuremberg Code's 10 Points.—It is puzzling to me, as a layman in legal matters, why the opinions expressed and the judgments rendered by the Nuremberg Military Tribunals concerning human experimentation cannot be construed as legal precedents (evidently not the case, cf. Ladimer [36a]) when they say that "certain basic principles must be observed in order to satisfy moral, ethical and legal concepts." At any rate, violation of these principles was considered as sufficient basis for imposing seven death sentences and nine prison terms. It would not seem unreasonable to conclude that, if "certain basic principles" (to be stated) are "satisfied," then "legality" shall have been attained. However that may be, the principles and the discussion of them are as follows.[37]

Nuremberg Rule 1: *The voluntary consent of the human subject is absolutely essential.*

This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiments.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

On first reading, this sounds simple, straightforward, and absolutely to the point. Reflection reveals certain difficulties. For one thing, a rigid interpretation of this would effectively cripple, if not eliminate, most research in the field of mental disease, which is one of the two or three greatest medical problems. However, Ivy served as chief medical consultant to the War Crimes Trials and presumably had a hand in formulating the 10 points. As he has said previously: "The ethical principles involved in the use of the mentally incompetent are the same as for mentally competent persons. The only difference involves the matter of consent. Since mental cases are likened to children in an ethical and legal sense, the consent of the guardian is required." [2] If this were the intention of the Nuremberg Tribunal, it is regrettable that the matter was not explicitly stated, for more and more the 10 points are referred to as a sort of Western credo.

We can consider what may be other difficulties in the way of widespread acceptance, difficulties not with the spirit and principal substance of the 10 points but difficulties, nonetheless, of interpretation.

Strict observance of point one would cast considerable doubt not only on the propriety of studying mental disease but also on the use of placebos, essential to progress in studies in which judgment is involved in decision.[18] Explicit observance of point one would require detailed explanation to the participating subject with the inevitable result that he would become self-conscious and introspective. An abundance of evidence in the field of study of subjective responses has shown that such introspection has produced misleading results.[5] The use of placebos in therapy, occasionally necessary for the guidance of the able, responsible physician as well as the treatment of the patient, could hardly be tolerated under a strict observance of the point in question.[9]

Furthermore, how is the investigator to draw a practical line in the prior information to be given his patient, between "reasonably to be expected" and possible hazards, when these will often be quite unknown in first experiments? Kety's [8] discussion of this question is, as usual, to the point:

In studies on normal individuals where there was no intent or little possibility of helping the subject, the rule of voluntary consent is, of course, absolutely essential and the necessity of complete explanation equally important. The completeness of the explanation, however, need refer only to that information which will enable the subject to make a judgment upon hazards and need not include other scientific information irrelevant to the question of risk and knowledge of which on the part of the subject may be prejudicial to a controlled experiment. In other words, if one were giving a potent drug or a placebo, it would be necessary to explain to the subject only the risks involved in the taking of the drug. In the case of patients there are important justifications for clinical research in addition to those which hold for normal controls. In the first place, if the research is relevant to the clinical condition from which the patient is suffering, and I feel that it should be, there is the clear possibility of personal benefit to the patient from the research itself, and there, perhaps, the criterion might be the chance of harming the patient versus the chance of helping him. Even though both of these chances may be low, in most clinical research the chance of personal benefit is usually considerably greater than the chance of harm to the individual patient.

With regard to the justification for using a placebo instead of a drug in the treatment of a disease, this can, of course, be justified if the purpose of the study is to evaluate a new and untried drug, since one can hardly be criticized for withholding an agent of unknown potential for good or harm. With regard to the question of withholding a drug of known benefit temporarily, the concept of greater harm versus greater good to the patient may still apply, in addition to which it may be perfectly possible to get the voluntary consent of the patient to cooperate in a research problem in which certain parts of the treatment may be delayed or withheld temporarily in order to make certain observations. In fact, in any case where the element of hazard is greater than the chances of benefit, the patient may still consent with full knowledge of the risk.

When a patient places himself in the hands of a physician for relief or cure of a symptom or disease, this act implies consent to the physician to carry out the necessary acceptable means to relieve or cure. If the problem is pain, for example, we know that a placebo will often relieve one-half to two-thirds of the pain relievable with an optimal dose of morphine.[39] Surely it would be carrying matters too far to require a dissertation to the patient on grades or degrees of relief anticipated, when real value could be expected from the use of a placebo. Such use of a placebo could reveal, for example, whether a powerful narcotic was actually necessary or not.

Possibly in the beginning, before its power to relieve was established, the use of a placebo in such work might have been challenged on ethical grounds more effectively than at present. This is true of many, if not most, standard therapeutic procedures in wide use today. In the early days of cardiac catheterization, that procedure could have been challenged on serious grounds as jeopardizing the immediate subject's life. Subsequently this has indeed been proved at times to be the case. At present, it is widely recognized that the demonstrated value of the technique outweighs the risk and this has been recognized by the award of a Nobel prize. Ladimer[39a] has described in chilling detail the probable fate in a court of law of the conscientious but bold investigator who takes such risks and experiences his failures early. In most cases, neither true risk nor benefit can be known early, and therefore they cannot be adequately described.

It is easy enough to say, as point one does, that the subject "should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision." Practically, this is often quite impossible, as we have seen, for the complexities of essential medical research have reached the point where the full implications and possible hazards cannot always be known to anyone and are often communicable only to a few informed investigators and sometimes not even to them. Certainly the full implications of work to be done are often not really communicable to lay subjects. As mentioned in an earlier section, this throws a serious burden on the responsible investigator. Once again, point one states a requirement very often impossible of fulfillment.

A further limitation on the matter of consent, as viewed by the Roman Catholic Church, has been expressed by Pope Pius XII [27]:

> In the first place it must be assumed that, as a private person, the doctor can take no measure or try no course of action without the consent of the patient. The doctor has no other rights or power over the patient than those which the latter gives him, explicitly or implicitly and tacitly. On his side, the patient cannot confer rights he does not possess. In this discussion the decisive point is the moral licitness of the right a patient has to dispose of himself. Here is the moral limit to the doctor's action taken with the consent of the patient.
>
> As for the patient, he is not absolute master of himself, of his body or of his soul. He cannot, therefore, freely dispose of himself as he pleases. Even the reason for which he acts is of itself neither sufficient nor determining. The patient is bound to the imminent teleology laid down by nature. He has the right of *use*, limited by natural finality, of the faculties and powers of his human nature. Because he is a user and not a proprietor, he does not have unlimited power to destroy or mutilate his body and its functions. Nevertheless, by virtue of the principle of totality, by virtue of his right to use the services of his organism as a whole, the patient can allow individual parts to be destroyed or mutilated when and to the extent necessary for the good of his being as a whole. He may do so to ensure his being's existence and to avoid or, naturally, to repair serious and lasting damage which cannot otherwise be avoided or repaired.
>
> The patient, then, has no right to involve his physical or psychic integrity in medical experiments or research when they entail serious destruction, mutilation, wounds or perils.
>
> Moreover, in exercising his right to dispose of himself, his faculties and his organs, the individual must observe the hierarchy of the orders of values—or within a single order of values, the hierarchy of particular rights—insofar as the rules of morality demand. Thus, for example, a man cannot perform on himself or allow doctors to perform acts of a physical or somatic nature which doubtless relieve heavy physical or psychic burdens or infirmities, but which bring about at the same time permanent abolition or considerable and durable diminution of his freedom, that is, of his human personality in its typical and characteristic function. Such an act degrades a man to the level of a being reacting only to acquire reflexes or to a living automaton. The moral law does not allow such a reversal of values. Here it sets up its limits to the "medical interests of the patient."

Brig. Gen. Telford Taylor,[40] who served as chief counsel for the prosecution of war criminals, says of the 10 points from the Nuremberg Trials that "the judgment lays down ten standards to which physicians must conform." Must? Most investigators would if they always knew how. Some of the foregoing discussion might be labeled as quibbling, but some is not. "The law is not concerned with trifles." It is at times difficult to distinguish between the two in a matter of this kind. Nothing said in this discussion should be construed as an attack on the principle of consent. The discussion is set down to indicate that even the "obvious" matter of consent is not so easy to live up to as it sounds.

Nuremberg Rule 2: *The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.*

The somewhat unsavory nature of the phrase "for the good of society" has been discussed previously. Point two is vague and frowns on random experiments; however, anesthesia, x-rays, radium, and penicillin, to mention a few products of "random" experimentation, seem to justify the disallowed approach. Most of the epoch-making discoveries in science have been unexpected.[41] Surely there is something to be said for the "random" experiment. I, at least, would not know how to define experiments "unnecessary in nature." Doubtless cardiac catheterization and frontal lobotomy would each have been placed in such a category at the beginning of their use. Perhaps lobotomy would be characterized by many in this way now, although it would not have been a few years ago. Decision is difficult; experiment clearly perilous.

Nuremberg Rule 3: *The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.*

But if the anticipated results fail to justify the performance of the experiment, has the investigator necessarily been guilty of wrong behavior? Who can guarantee the success of any new experiment?

The aforementioned comments are by no means intended to scoff at this valiant effort to codify permissible experimentation in man. They are intended, rather, to indicate more clearly than the 10 points do how difficult it is to be precise in this field. The remaining seven points will be set down without comment.

Nuremberg Rule 4: *The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.*

Nuremberg Rule 5: *No experiment should be conducted where there is an* a priori *reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.*

Nuremberg Rule 6: *The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.*

Nuremberg Rule 7: *Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.*

Nuremberg Rule 8: *The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.*

Nuremberg Rule 9: *During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.*

Nuremberg Rule 10: *During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.*

Notwithstanding the difficulties of formulating rules to cover all occasions, it was clear from the principles set down at Nuremberg [37] that during the war

these ten principles were much more frequently honored in their breach than in their observance. Many of the concentration camp inmates who were the victims of these atrocities were citizens of countries other than the German Reich. They were non-German nationals, including Jews and "asocial persons," both prisoners of war and civilians, who had been imprisoned and forced to submit to these tortures and barbarities without so much as a semblance of trial. In every single instance appearing in the record, subjects were used who did not consent to the experiments; indeed, as to some experiments, it is not even contended by the defendants that the subjects occupied the status of volunteers. In no case was the experimental subject at liberty of his own free choice to withdraw from any experiment. In many cases experiments were performed by unqualified persons; were conducted at random for no adequate scientific reason, and under revolting physical conditions. All of the experiments were conducted with unnecessary suffering and injury and but very little, if any, precautions were taken to protect or safeguard the human subjects from the possibilities of injury, disability, or death. In every one of the experiments the subjects experienced extreme pain or torture, and in most of them they suffered permanent injury, mutilation, or death, either as a direct result of the experiments or because of lack of adequate follow-up care.

Declarations of Geneva and Rome.—The declarations of Geneva and Rome, which have been adopted by the World Medical Association, consist of a rephrasing and amplification of the Hippocratic oath.[42] Nothing is said directly about experimentation; however, in the section on "Duties of Doctors in General," the following statement could be considered as a limitation of experimentation: "Under no circumstances is a doctor permitted to do anything that would weaken the physical or mental resistance of a human being, except for strictly therapeutic or prophylactic indications imposed in the interest of the patient."

Views of the United States Public Health Service.—The United States Public Health Service has, in effect, adopted the Nuremberg Code's 10 points, with added comment on the importance of group review and group approval of all procedures when even remote possibilities for hazard exist.[7] The rights and welfare of the patient are emphasized.

Concerning research patients at the Clinical Center for Medical Research of the United States Public Health Service, Topping [43] has said:

An overriding principle governing our clinical studies is that the welfare of individual human beings takes precedence over every other consideration. Medical procedures or therapy substantially different from accepted general medical practices are often an essential component of clinical medical

research. This offers the only means of acquiring certain information necessary to solve the problems of the diseases and disorders that afflict man. Ethical and scientific considerations dictate, however, that these investigations must be undertaken only after mature thought, under rigorously defined and controlled conditions, and under circumstances that will minimize the dangers of predictable or unpredictable hazards. The basic principle on which all such investigations must rest is that human beings have inalienable rights that supersede all other considerations that may be raised in the name either of science or of the general public welfare. The responsibility of the physician for the physical and mental well-being of persons in his care and for observance of the ethics of his profession cannot be overridden by any element of study or research that is interjected into the relationship between the physician or surgeon and persons in his care.

Views of French Academies.—The National Academy of Medicine, of France,[44] points to the need for a distinction between (1) investigation and therapy directed toward the patient's health as the right and duty of the physician, "conducted with the necessary prudence and following the rules of medical ethics," and (2) research with other ends in view. In this case, in which the experimentation is "for scientific purposes only" it is essential that (1) only true volunteers who are informed concerning the project be used and that (2) the investigators be well qualified for the task at hand and thus reduce the hazard to a minimum.

The view of the French Academy of Moral and Political Sciences is that only responsible, experienced scientists should engage in human experimentation, men who can be expected to draw their own prudent limits to their activities, for written law of itself cannot provide an adequate safeguard. The final justification for such work is the scientific knowledge gained.[45]

British Views.—British views on this subject have been stated by J. M. Mackintosh,[46] a British scientist acting as special consultant to the United States Public Health Service. He has made the following points: Consent is essential by the individual or his guardian.

> The law in England is by no means clear as to the responsibility of the experimenter in the case of accident arising. The maxim "volenti non fit injuria" still holds, and might be freely expressed as "volunteers can't claim damages." But, of course, experimental research on sick persons designed to elucidate the nature of their disease and to provide treatment is well established. There has been a movement of late, however, to invite sick persons to cooperate in physical experiments upon themselves with the primary object of elucidating some fundamental problem of disease, without necessarily affecting their individual treatment. [Mackintosh points out that the consent] of a patient as a member of a research team acting as it were the part of the donor in the experiment, is new and startling. . . . Whether this cooperation in the event of accident is covered by the consent in writing of the patient is a matter which would have to be tested in the courts. Obviously the patient would be protected in common law here, as elsewhere, against negligence. But suppose no negligence has occurred, and in consequence of an experiment—the outcome of which cannot be known—a patient suffers a damage or death. The position of the director of the team and of its members would stand in some doubt. It is clear that the law would have to require 1) that the patient had been clearly informed of the nature and purpose of the experiment and of any results that it might involve; 2) that the experiment had been carried out not merely without negligence but with every available precaution against disaster, (e. g., by the provision of restorative apparatus); and 3) that the person responsible for the experiment was a person who could in the eyes of the law be confidently entrusted with the important tasks which he was undertaking. In this respect, it is evident that in addition to any expertly qualified scientist, a physician of standing would have to subscribe to the responsibility of the team.

Mackintosh [46] recognizes two ways of safeguarding the patient after the aforementioned propositions are accepted. This can be either by "an elaborate and meticulously worded code of regulations designed to cover the whole pattern of situations which might occur," or, abandoning any attempt to use a code of regulations, by the use of a "carefully worded 'statement of faith' on the ethical question of research." He expresses as his personal view that "the mere preparation of a closely defined code of regulations would defeat its own purpose. Human beings are not alike, and a code of regulations obeyed to the letter by one research worker might well result in irretrievable damage of a patient. There is no code that could cover the frailties of an inefficient worker, or the sinister vagaries of a research student who placed his own ambitions above the human needs and rights of the patient."

The British Medical Research Council [10] has also said, "it is impossible to frame a code of general advice which would adequately cover the ever changing circumstances which arise."

Views of the Roman Catholic Church.—Pope Pius XII [27] has said:

> Sometimes it happens that a method cannot be used without injuring the rights of others or without violating some moral rule of absolute value. In such a case, although one rightly envisages and pursues the increase of knowledge, morally the method is not admissible. Why not? Because science is not the highest value, that to which all other orders of values—or in the same order of value, all particular values—should be subordinated. Science itself, therefore, as well as its research and acquisitions, must be inserted in the order of values. Here there are well defined limits which even medical science cannot transgress without violating higher moral rules. The confidential relations between doctor and patient, the personal right of the patient to the life of his body and soul in its psychic and moral integrity are just some of the many values superior to scientific interest. This point will become more obvious as We proceed.
>
> Without doubt, before giving moral authorization to the use of new methods, one cannot ask that any danger or any risk be excluded. That would exceed human possibilities, paralyze all serious scientific research and very frequently be to the detriment of the patient. In these cases the weighing of the danger must be left to the judgment of the tried and competent doctor. Nevertheless, as Our explanation has shown, there is a degree of danger that morality cannot allow. In doubtful cases, when means already known have failed, it may happen that a new method still insufficiently tried offers, together with very dangerous elements, appre-

ciable chances of success. If the patient gives his consent, the use of the procedure in question is licit. But this way of acting cannot be upheld as a line of conduct in normal cases.

People will perhaps object that the ideas set forth here present a serious obstacle to scientific research and work. Nevertheless, the limits We have outlined are not by definition an obstacle to progress. The field of medicine cannot be different in this respect from other fields of man's research, investigations and work. The great moral demands force the impetuous flow of human thought and will to flow, like water from the mountains, into certain channels. They contain the flow to increase its efficiency and usefulness. They dam it so that it does not overflow and cause ravages that can never be compensated for by the special good it seeks. In appearance, moral demands are a brake. In fact, they contribute to the best and most beautiful of what man has produced for science, the individual and the community.

Requirements of the American Medical Association.—The American Medical Association [38a] has three principal requirements: "(1) the voluntary consent of the person on whom the experiment is to be performed; (2) the danger of each experiment must be previously investigated by animal experimentation, and (3) the experiment must be performed under proper medical protection and management." This is, in essence, similar to the Nuremberg document, and the comments appended to that are pertinent here.

Wiggers' Statements.—In effect, Wiggers [9] restated the 10 points of the Nuremberg Code, with extensions or additions as follows:

1. Human experiments should not be projected until their necessity has been unquestionably established and a feasible humane procedure for their conduct has been formulated.

2. The scientific, ethical, and legal considerations pertaining to contemplated studies on human subjects should, whenever possible, be reviewed and approved by a group of colleagues who will not participate in the investigation. The nature of the experiments and reasons for their performance should be explained.

8. The investigation should be so conducted that legal liability under malpractice or personal injury laws never comes into question.

To follow Wiggers' point one concerning necessity would, of course, be proper if danger attended the proposal. In experiments devoid of hazard it is difficult to see why the experimenter should not have freedom to try out his hunches, provided that the subjects understand the uncertain nature of the project and give consent. Many of the great discoveries of science have come from just such "unnecessary" and "random" experimentation.[41] Regarding point eight, as the laws are now written and at present interpreted,[36a] it seems clear that the investigator is frequently, if not always, in danger of being subjected to "legal liability under malpractice or personal injury laws."

World Medical Association.—The World Medical Association has presented a summary of a long report prepared by the Public Health Council of the Netherlands, which was submitted to that country's Minister of Social Affairs and Health on Oct. 10, 1955. After defining human experimentation as any "intervention in the psychic and/or somatic integrity of man which exceeds in nature or extent those in common practice," the report presents an elaborating discussion and summary of reasonable practices already discussed.

Approval of the Subject. It is generally agreed that if the experiment is not solely, primarily, or to any degree a direct benefit to the subject, his approval is required. This approval should neither be conditioned by idealistic impulses, (nurses and medical students); nor by special conditions, (prisoners, etc.). Even under ideal conditions, the subject's consent has only relative importance.

However the committee felt that when a physician undertakes "new treatment" on his own patient, the relationship of confidence between physician and patient is in no way violated if the physician increases his knowledge or experience without first informing the patient, with the understanding that recovery is not delayed and there is no detrimental effect.

After all, hospitals exist not only to treat patients, but also to increase medical knowledge and skill. Animal experimentation always precedes that on humans. The public should understand that the interests of the patients require a certain amount of experimentation.

Risk. "Risk" is defined as "any danger that is greater than the inevitable peril." Surgical procedures inevitably involve a risk, therefore, proper investigation and use of powerful new medicaments cannot be carried out without a degree of inevitable risk to the patient.

A distinction is made between the research expert and the investigator who is also the patient's attending physician. The Committee was of the opinion that "medical activities involving risk to the experimental subject should not be carried on by the practicing physician; the practicing physician who also is the investigator is not the person qualified to objectively judge the risk involved."

When experimentation is conducted in institutions such as homes for children, convalescents or old people, etc., the responsibility must be shared by the attending physician in addition to the investigator.

The Committee recognizes the inherent right of a person to accept a voluntary risk, and the right of the investigator to make use of this attitude to achieve altruistic objectives but ethics must act as a check wherever a great risk is involved. Dangerous experiments are never justifiable if the aim is only advancement of medical knowledge; they must also entail some benefit for humanity.

The Committee recognized that in time of war or epidemic, dangerous experiments may be justified. However, in normal times, "human experiments involving dangerous risks of life cannot be reconciled with the nature and objective of the medical profession." Hence it recognized that the nature of this problem does not make it possible to have clearly defined standards governing experimentation; "the conscience of the investigator will have to determine the course of conduct" and even the "individual conscience cannot be relied upon unconditionally." . . . For, "scientific experimentations demand from the investigator an objective attitude, a certain distance and restraint toward his object of experimentation which is actually in conflict with the relationship of physician and patient."

Standards. Nevertheless, it is felt that standards should be sought that will govern individual conscience in making decisions; guarantee acceptable scientific procedures; and provide all the precautions necessary.

The Committee recommends the following guarantees and standards:

a. Study of relevant publications to avoid unnecessary repetitions of experiments;

b. The physicians conducting experiments should have special knowledge of the problem and be completely responsible;

c. Good organization and execution;

d. Every available aid for special or emergency treatment of the experimental subject should be available.

Prior to experimentation the following aspects should be considered:

1. Can the experiment, wholly or partly, be carried out on animals?

2. What is the minimum requirement to obtain the observation? Is its importance and durations ethically justifiable?

3. What is the minimum requirement in altering the conditions of the experiment?

4. Are the requirements for the observation and the alterations of conditions the same?

5. What arrangements are planned? Is the project the fruit of mature thought and expert advice?

6. How will the results be used in obtaining a definite conclusion?

Risk, inconvenience or pain for the subject should be governed by these principles:

a. The investigator's responsibility is more important than the willingness of the subject to accept the conditions;

b. The investigator should consult other experts on the research project in order to intensify the sense of responsibility;

c. The subject must be fully informed and must consent freely;

d. If considerable risk is involved, the experiment is not in accord with the object and purpose of medicine;

e. A practicing physician should not become an investigator on his own patient, if the experiment involves danger. A body of advisers should be consulted;

f. Experiments should be discontinued if the subject so desires or if unexpected danger is encountered, activities the consequences of which cannot be undone, and which therefore cannot be discontinued, are therefore disapproved;

g. Any suffering or danger not strictly inevitable must be prevented;

h. Experiments on children; in institutions for children, old people, etc.; on the insane; or on prisoners, which involve dangerous risks, inconvenience or pain are not approved. All experiments on the dying under any circumstance are disapproved;

i. The "utmost restraint" must be exercised in experiments on patients deemed to have an incurable malady, even though they volunteer as subjects;

j. Unnnecessary examinations should be avoided, and diagnostic activities that may be dangerous are justified only if they result in effective therapy. In routine examinations new methods that are dangerous should be strictly limited.

The following additions are suggested: 1. Patients who are soon to die or who are in imminent danger of death should not be considered suitable subjects for research unless it is intended to benefit themselves. Potentially useful procedures might thus be unjustly blamed and the reputation of the investigator be damaged. 2. As a general principle, subjects with an unrelated disease should not be utilized for investigation involving another disease.

The principle codes have been presented above. The armed services in the United States and one or two state organizations abroad have classified codes which cannot be quoted. Such codes as I have seen do not contain anything not presented here.

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PORENCEPHALY.—The term porencephaly is used to indicate nontumorous cystic lesions of the brain communicating with the ventricles and/or the subarachnoid space, resulting from either developmental or destructive lesions. It is not possible to assign each case to one or the other pathogenic group on a clinical basis. The large majority of the cases presented belong to the group of destructive lesions, or "encephaloclastic porencephalies." . . . The cases in which symmetrical bilateral frontal cysts were demonstrated is the only one which can reasonably be considered as belonging to the developmental, or "schizencephalic," group. We have limited the use of the term porencephaly to those cases in which the etiological lesion occurred prior to, incidental to, or shortly after birth. The clinical features of porencephaly as a disease consist, in a majority of instances, of symptoms referable to a focal cerebral hemispheric lesion, with the clinical onset at a variable time after occurrence of the underlying process, and developing with an accumulative and progressively severe course. In most cases of porencephaly the signs are indicative of focal cerebral lesions which correlate well with the symptoms. The clinical picture, in the majority of patients, early in its course, is mild to moderate in degree, so that it does not precipitate adequate study until adolescence or early adulthood. The only symptoms that apparently improve were seizures of various types, which did so after excision of the cysts or upon adequate anticonvulsive therapy. The pathogenic changes which account for the clinically progressive characteristics of this disease remain to be disclosed and explained.—R. W. Naef, M.D., Clinical Features of Porencepaly, *A. M. A. Archives of Neurology and Psychiatry*, August, 1958.

CHEMICAL LABORATORY

The following paper has been authorized for publication by the Chemical Laboratory.
WALTER WOLMAN, PH.D., *Director.*

IDENTIFICATION GUIDE FOR SOLID DOSAGE FORMS

John J. Hefferren, Ph.D., Chicago

The need to identify rapidly an unknown tablet or capsule frequently occurs in a wide variety of circumstances. In such cases, a qualitative chemical analysis followed by confirmation tests frequently is a long and difficult task. The time factor, coupled with the limited quantities of the unknown, makes the identification difficult and often impossible.

Methods to aid in identification have involved direct comparisons of the unknown with pictures of known products [1] or with authentic samples carried on various types of display boards. Such methods may suggest the identity of the unknown or eliminate a few possibilities, and in this way they are of some value in identification work but are necessarily limited in scope.

Development of Identity Guide

As a possible aid in drug dosage identification work occasionally undertaken by the A. M. A. Chemical Laboratory, the feasibility of a preliminary screening method, based solely on the physical characteristics of solid drug dosage forms such as tablets and capsules, was investigated. Examination of a number of commercial tablets and capsules quickly made it evident that there were sufficient differences in the several physical characteristics to suggest reliance on them in an identification or screening procedure. To test these initial observations, 100 products were examined and catalogued according to their physical characteristics.

Since the results were encouraging, the study was then extended to 500 samples. These samples, including both prescription and proprietary drugs, were obtained from the drug files of the Chemical Laboratory, physician's samples, and from a commercial drug store. The samples were not selected according to any use-frequency statistics but on the basis of a representative cross section of the physical characteristics of the tablets and capsules.

From the experience gained in examining these 500 products, a dosage identification guide was developed. This system helps one to identify an unknown by following through a series of categories of physical characteristics, with the consequent elimination of many individual drug preparations and the eventual restriction of remaining possibilities to a relative few.

After completion of this pilot study with the 500 products, the dosage identification guide was discussed in detail with representatives of various agencies and specialty groups concerning the feasibility and need for such a scheme in their particular areas. These included physicians, personnel in emergency receiving rooms, the A. M. A. Committee on Toxicology, toxicologists, pharmacists, and medical examiners and representatives of government agencies, poison control centers, the pharmaceutical industry, and law enforcement agencies.

These conferences indicated that such a suggested guide would prove valuable in a number of areas, provided it were available in suitable form. It is planned to make this information available by publication of a text which would include a short discussion of the dosage identification guide, general information on solid drug dosage forms, a set of color reference chips, and data on the physical characteristics of those products examined.

Solid Dosage Identification System

This dosage identification guide (fig. 1) is constructed to accommodate all the individual tablet and capsule preparations on the market. The guide has three main categories: tablets, soft gelatin capsules, and hard gelatin capsules. In each of these categories is listed a number of terms to describe the individual characteristic under such headings as coating, shape, coloring, contents, markings, scoring, and size.

The shapes of the various tablets and capsules used in the dosage identification guide are illustrated in figure 2. When the tablets are viewed from the side, one of the most characteristic differences between sugar-coated, uncoated, and film-coated tablets is easily seen. Since sugar-coated (pan-coated) tablets are coated by tumbling, all the ridges resulting from compression of the core are rounded by subsequent layers of coating material. Film-coated tablets are coated by dipping; thus, they have a thin film coat but retain ridges characteristic of the uncoated tablet. Some forms of sugar-coated tablets are quite similar to soft

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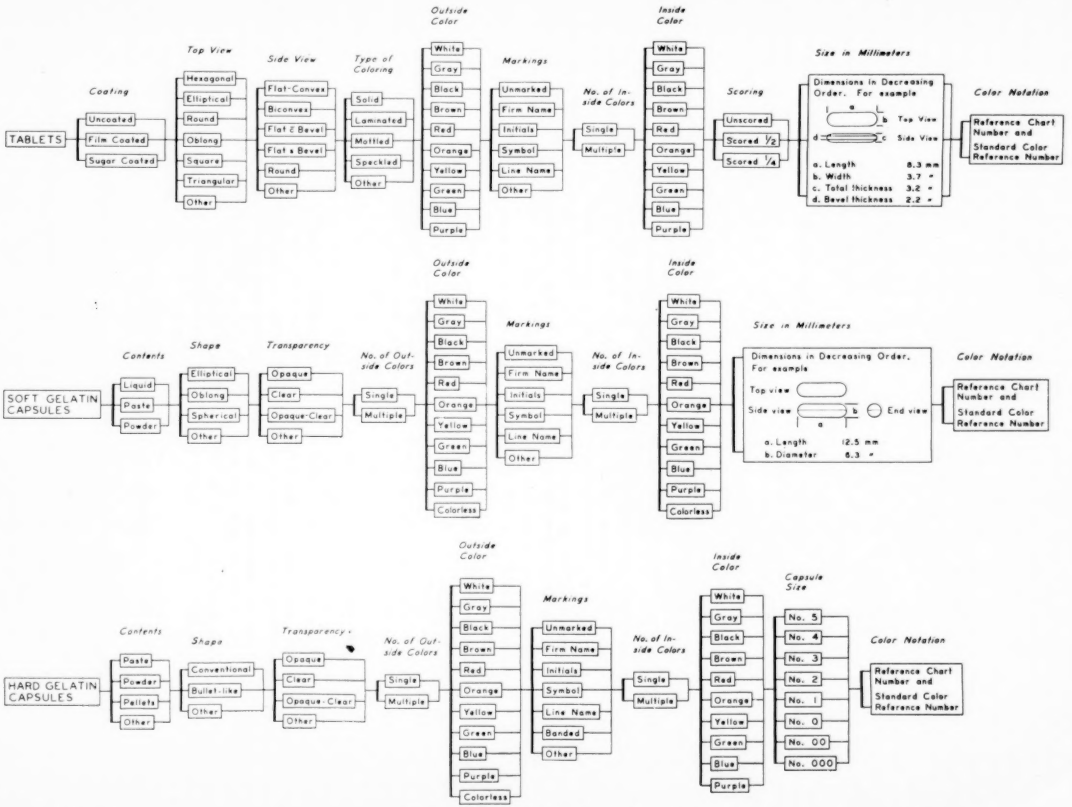


Fig. 1.—Dosage identification guide.

gelatin capsules. The essential differences are that the soft gelatin capsule has a seam at the point of closure of the two halves, and the contents can be liquid, paste, or powder. The sugar-coated tablet will not have a seam and will have a compressed core.

In the dosage identification guide (fig. 1), the outside and inside color categories have 10 terms for tablets and 11 for capsules. The use of a limited number of colors at this point in the guide is to facilitate indexing. At the far right of the guide is provision for a more exact color notation of the product.

A more exact color notation is obtained by comparison of the colors of the product with a set of reference color chips, which will be included with the identification text. For example, a sugar-coated tablet might be described by using the limited color terms as outside color, red, and inside color, brown,

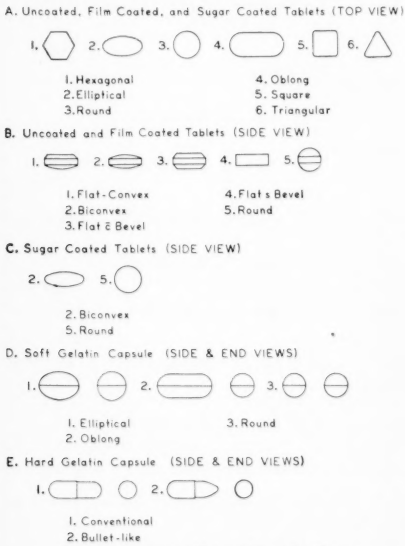


Fig. 2.—Common tablet and capsule shapes.

whereas in the color notation category, these two colors might be more accurately described in relation to the reference chips as red no. 2 and tan no. 1 respectively.

The color of each product will also be notated by reference to a commercially available color text. This information will be of value only to those who have that text and would constitute an auxiliary refinement of the identification guide. This additional color notation system would not be necessary for the normal use of the system.

The data reported for the dimensions of tablets and capsules are subject to three sources of variation. They are variation due to (1) manufacture, (2) limitations of the measuring device, and (3)

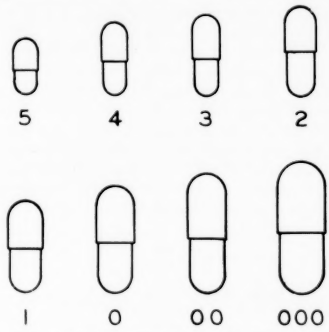


Fig. 3.—Standard capsule sizes (actual size).

precision of the measurements. The magnitude of these sources of variability will be dependent, in part, on the particular type of tablet or capsule.

Due to its method of manufacture, the size of an uncoated (pressed powder) tablet is most readily reproduced within the same lot and between lots. The diameter of such a tablet is determined by the diameter of the die used in the compression of the tablet and is usually duplicated to within 0.1 mm. On the other hand, the total thickness is a

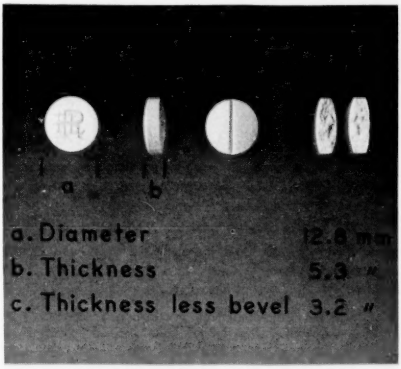


Fig. 4.—Physical characteristics of sample tablet.

less accurate dimension because of manufacturing variables such as granulation density. The duplication of this dimension, however, is usually within 0.3 mm., depending to some extent on the size of the tablet. The measurement at the bevel edge is

related to and has the same variables as that of the total thickness, plus the added variable due to greater difficulty in obtaining as accurate a reading at the edge with a measuring device. With uncoated, pressed powder tablets, the dimensions in decreasing order of reproducibility are diameter, total thickness, and bevel thickness.

With film-coated and sugar-coated tablets and soft gelatin capsules, a wider range of dimensional variability results because of the methods of manufacture. These products (with the exception of film-coated tablets) do not have a bevel measurement and as a result have one less dimension than does the comparable shape in an uncoated tablet. Thus, the dimensions of film-coated and sugar-coated tablets and soft gelatin capsules are somewhat less definitive than are those of an uncoated tablet; however, this is somewhat offset by the many colors and types of contents which these products usually have.

All measurements of tablets and soft gelatin capsules are made with a vernier calipers reading to 0.1 mm. The size of a hard gelatin capsule is determined by comparison to a chart of standard capsule sizes (fig. 3). These capsule sizes are accepted throughout the pharmaceutical industry and represent the most convenient way to describe the size of a hard gelatin capsule.

Application of Dosage Identification Guide

To illustrate the application of the dosage identification guide to a specific problem of identification, the commercially available tablet pictured in figure 4 can be used as an example of an unknown. Using the guide, figure 1, the term best describing this tablet in each category such as coating, top view, etc., is selected. For this tablet, the terms and the corresponding categories of physical classification would be as follows:

Coating ..... uncoated	No. of inside colors .... single
Top view ..... round	Inside color ..... white
Side view ..... biconvex	Scoring ..... scored-½
Type of coating ..... solid	Dimensions 12.8, 5.3, 3.2 mm.
Outside color ..... white	Color notation ..... white
Markings ..... initials	

After the selection of those terms best describing the physical characteristics of this tablet, the text containing similarly obtained listings for commercially available tablets and capsules is referred to for the possible solution to the identity of the unknown. An abbreviated and idealized page of this text might look like that shown in figure 5. This page contains a listing of tablets which are uncoated, round, biconvex, white, marked, and scored-½. The third product listed has the same physical characteristics, markings, and dimensions as the tablet in figure 4, so the tablet is probably the 0.5-Gm. tablet of sulfisoxazole (Gantrisin) manufactured by Hoffmann-LaRoche. Positive identification of this tablet should then be made by some confirmatory test.

In figure 6, the application of this guide and text to 500 products demonstrated its workability with a variety of tablets and capsules, ranging from the unusually shaped, well-marked products to the

— TABLETS —

Uncoated, Round, Biconvex, White, Scored-½, Marked

MARKINGS	SIZE IN mm	TRADE NAME	DOSAGE	FIRM
A	7.2 3.0 1.4	Theruhistin	4 mg.	Ayerst
A	6.4 2.6 1.0	Arlidin	6 mg.	Arlington Funk
HR	12.8 5.3 3.2	Gantrisin	0.5 gm.	Hoffmann LaRoche
W	8.0 4.0 2.3	Hedulin	50 mg.	Walker
U	6.4 2.7 1.8	Delta-Cortef	5 mg.	Upjohn
RIKER	11.2 5.3 3.2	Calcium Disodium Versenate	0.5 gm.	Riker
TABLOID BRAND	7.5 3.1 2.0	Daraprim	25 mg.	Burroughs Wellcome

Fig. 5.—Idealized page of future text on identification of solid dosage forms.

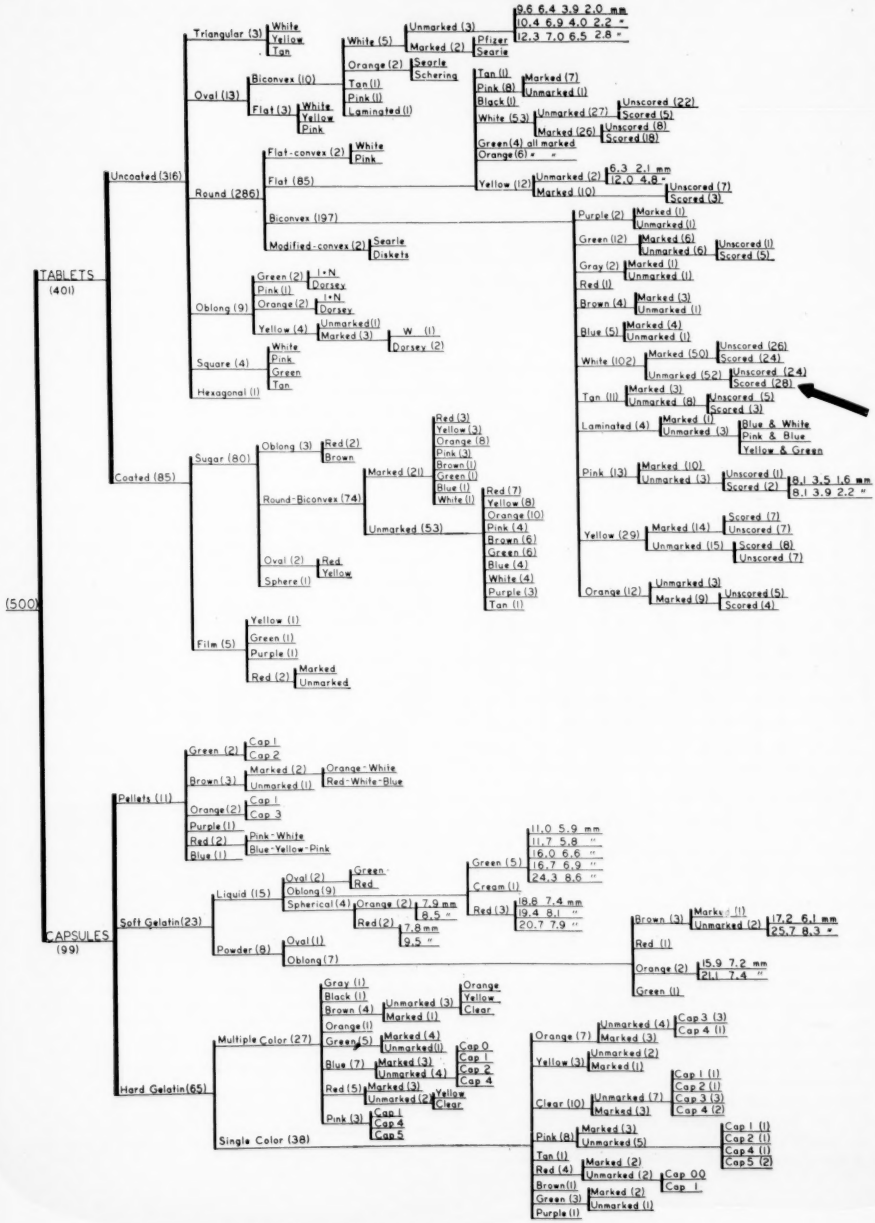


Fig. 6.—Breakdown of 500 products used in pilot study.

familiarly shaped, unmarked products. Proceeding from left to right across the chart, gradual elimination or separation of the 500 products into groups occurs. The numbers in parentheses on the chart represent the number of individual products remaining in that group.

At the far right of the chart, wherever the breakdown ends as marked products, there are still two further aids to identification, that is, the dimensions and the actual markings such as symbols, initials, or names. In these cases complete separation usually occurs, leaving no two products in the group alike in every physical characteristic utilized by the coding system.

On the other hand, the unmarked categories, such as that indicated by the arrow in figure 6, can be further separated only on the basis of size. This tablet group—uncoated, round, biconvex, white, unmarked, and scored-½—contains 28 products, which is the largest group in the sampling of 500 products.

1	2	3	1	2	3
8.0	3.0	1.2	10.5	4.5	2.6
8.0	3.5	2.0	10.5	4.9	2.4
8.0	3.7	2.0	10.6	4.8	2.8
8.0	4.3	2.1	11.1	4.6	2.5
8.8	3.6	1.9	11.1	5.9	3.9
8.8	3.6	2.0	11.2	4.9	3.2
8.8	3.7	2.0	11.2	5.0	3.1
8.9	3.4	1.5	11.2	5.4	3.4
9.6	4.3	2.3	11.2	5.9	4.2
10.4	4.3	2.3	12.8	5.0	3.0
10.4	4.4	2.5	12.8	5.1	3.0
10.4	4.5	2.6	12.8	5.6	2.6
10.5	4.0	2.0	16.0	6.7	4.0
10.5	4.4	2.4	17.7	8.7	3.4

1 - Diameter in mm, 2 - Thickness in mm, 3 - Bevel Thickness in mm

Fig. 7.—Dimensions of uncoated, round, biconvex, white, unmarked, and scored-½ tablets.

The sizes of these 28 products are listed in figure 7. The first 4 of these products have the same diameter of 8.0 mm., whereas the other 24 products are sufficiently different to be eliminated by this first measurement. The thickness of the first and fourth separate them from the second and third products; however, the third measurement fails to achieve any further separation. Reference to the text will indicate what the drug compositions may be. Identification is then relatively simple by application of confirmatory tests for these substances.

There are eight tablets in figure 7 with a diameter between 10.4 mm. and 10.6 mm. Thickness measurements eliminate three of these products (4.0, 4.8, 4.9); thus, the remaining five represent 1% of the 500 products used in this initial study. It is recognized that when thousands of samples instead of 500 are examined and coded into the scheme, the total number of individual products in such a nondistinguishable group will be much greater, even though the percentage of the total may not change.

Present Status

The examination and coding of commercial drug products is under way. A list and samples of those drugs which represent approximately 87% of the prescription drugs used have been obtained and coded. The same approach is being applied to the proprietary drugs. With these most frequently used drugs as a core, coding is extending to other commercially available tablets and capsules.

Extension of the coding system to include other solid drug dosage forms such as suppositories is planned. Some nondrug products such as plant foods, which are now commercially available in tablets and capsules, will also be included.

It is planned that all the data obtained from coding the physical characteristics of these products will be organized and published in text form together with the dosage identification guide, color reference chips, and instructions for use. It is hoped that the first edition of this text including some 5,000 listings will be published in about a year. Thereafter, supplements and new editions will be published to include new products and those old products whose physical characteristics will have been changed. Further editions will be expanded then to include all the commercial drug products obtainable.

The success of this project depends on obtaining authentic drug samples. This is one of the most difficult problems in this work, and it is hoped that samples will be made available to us by the many firms, individuals, and agencies who have such products. At least six individual tablets and capsules of each size, the name of the product and of the manufacturer, and dosage size are essential for coding purposes.

The color reference chips used in the text will be selected and prepared with the assistance and advice of Mr. Carl Foss, Princeton, N. J.

The list representing 87% of prescription drugs used in this study was developed and contributed by Mr. David D. Stiles of Abbott Laboratories, North Chicago, Ill., from a prescription survey project carried out under his direction.

The samples of these prescription drugs were gathered and contributed by Sargent's Drug Stores, Inc., Chicago, through the courtesy of Mr. William Morse.

Reference

1. Tablet and Capsule Identification Guide, 1956, Chemist and Druggist: Annual Special Issue, pp. 603-606, June 30, 1956; Tablet Identification 1958, ibid., pp. 698-703, June 28, 1958.

Cost of Medical Care

As the American's income has risen, so has his annual expenditure for individual health services—only more so. The Health Information Foundation last month reported that, whereas 3.7% of the consumer-expenditure dollar went for health services in 1929, the comparable 1957 figure was 5.3%.

HIF attributes this to two facts: the quantity and variety of private health services and the vastly improved quality. The foundation stated: "Pain, disability, and serious illness could be faced at relatively little expense in the past because there was little that could be done for a sick person. Now pain and disability can often be avoided, and death greatly postponed—but at the cost of more visits to physicians, more admission to hospitals, more use of drugs and other treatments."

Not only has the gross amount spent for these health services increased (to 15 billion dollars in 1957), according to HIF, but the proportionate share spent for insurance, drugs, and hospital and professional services has undergone revision.

The foundation states, for example, that physicians' services took almost 33 cents out of the 1929 medical care dollar, whereas by 1957 this share dropped to less than 25 cents. Conversely, says HIF, hospitals in 1929 were receiving less than 14 cents, but by 1957 were taking almost 26 cents of that dollar.

MEDICINE AT WORK

- *People and Crashes*
- *Ahead in Mental Health*
- *Saving for Medical Bills*
- *Worker Health Survey*
- *The Moon Is 'Old Hat'*
- *Talk with Pioneer Space Doctor*

A. M. A. Committee in discussion of auto safety last month. Left to right are Drs. Horace Campbell, John Rodger, James Goddard, Charles Hayman (guest participant), Jacob Kulowski, and (back to camera) Fletcher Woodward, chairman.

—J. A. M. A. photo

Human Inadequacy—Is It the Vital Clue to Safety on the Highway?

> "Only a mass of crumpled metal that once had been an automobile remained today to offer mute testimony to the speed with which a salesman's car struck a freight train last night. . . . ." (Illinois)
>
> "Four teen agers died today as the car in which they were riding ran head on into a semi-trailer truck on a mountain road. . . . ." (Colorado)
>
> "Seven lost their lives and two more were injured yesterday in a collision that resulted when two cars, traveling in opposite directions, attempted simultaneously to pass the vehicles in front of them on a three-lane highway. . . . ." (Indiana)

News stories such as these daily record the terrible toll of highway tragedy that has become an almost accepted part of the American scene. Night or day, main highway or back road, kids in their teens or a pair of grandparents—day after day the slaughter has continued virtually unchecked to reach an estimated total last year of 37,000 dead; another one and one-third million with disabling injuries. The motor vehicle, which as much as any single invention brought Americans to their peak of material comfort, has also brought a record of death and crippling injury so staggering that one writer even pointed out its efficacy as a method of population control.

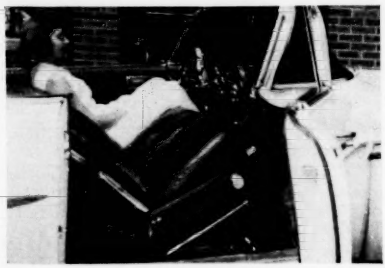
One group that two years ago sank its teeth into the accident problem was the A. M. A.'s Special Committee on Medical Aspects of Automobile Injuries and Deaths (see Medicine at Work, THE JOURNAL, Oct. 27, 1956). Its Chairman, Dr. Fletcher Woodward of Charlottesville, Va., reduced the problem to its essentials when he wrote: "The highway traffic accident problem has three main components—the driver, the highway, and the vehicle. Today, human failure overshadows all other factors in the production of highway accidents."

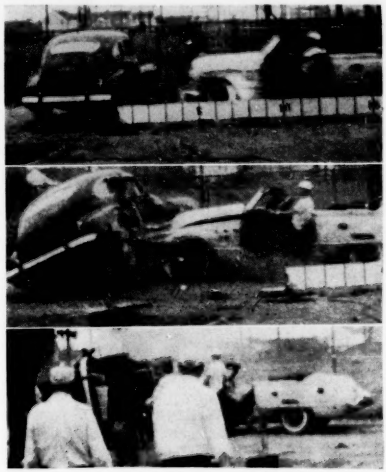
Guides to Driving Ability

Starting with this basic assumption, the Committee has spent its first two years in the production of three guides. One-half million copies of the Committee's 15-page booklet, "Are You Fit to Drive?" have been made available to the public through physicians and insurance companies. Colorfully illustrated, it outlines a series of conditions that affect individual capacity to operate a motor vehicle. More explicit and comprehensive is the soon-to-be-published "Medical Guide for Physicians in Determining Fitness to Drive a Motor Vehicle" which received a final polish when the Committee met in Chicago last month.

Both publications deal—as will the forthcoming "Medical Guide for

A bumper-triggered, hydraulic system that pulls the driver's seat forward and tilts it to the rear with a scooping motion in 0.0031 of a second is being offered as a possible antidote to front-end collision injuries. The device allows front-seat passengers to take impact force on their hindquarters. The system, manufactured by Protect-O-Matic Corp., was demonstrated in an action film on test crashes (*right*) shown last month to the A. M. A. Committee on Medical Aspects of Automobile Injuries and Deaths. Test drivers have emerged uninjured in 50-mph collisions, the manufacturer claims.





Licensing Authorities"—with physical, emotional, and toxicological states that affect individual competence behind the wheel. The "Medical Guide for Physicians" states: "The physician is the person best able to ascertain the physical, mental, emotional, or physiological impairments of an individual. Moreover, he is in a good position to evaluate these impairments in relation to safe driving ability."

How much of a role does the physical and mental condition of a driver play in highway accidents? Nobody knows for sure, but there have been some informed guesses. Capt. R. C. Blossom, research and development officer of the California Highway Patrol, offered one last summer when he spoke at the A. M. A.'s Annual Meeting in San Francisco. He said: "An analysis of coroners' reports covering 653 motor vehicle deaths indicates 62 may have been due to natural causes. From this small sample, plus logic, it would appear that existing and induced physiological conditions of drivers involved in fatal auto accidents may constitute a major portion of the true causes of death in an automobile."

With its three guides, the Committee hopes in time to be able to discourage persons with potential disabilities from operating motor vehicles. In addition, members of the Committee have written, and in some cases testified before legislative bodies, of the value of safety design in motor cars, the need for seat belts, and the dangerous impact of even limited alcohol usage on driving ability.

Others Work for Safety

Other new and continuing efforts include:

—The A. M. A. joined with the National Safety Council and the Public Health Service last month to revive flagging interest in the injury-reducing potential of seat belts for passenger cars.

—A 14-man team from the Department of Legal Medicine of the Harvard Medical School this month began a five-year study of fatal auto accidents supported by an $809,000 federal grant. Efforts will be made to trace the erring motorist's physical and psychological history to determine factors that may have affected his driving ability.

These efforts all have one thing in common. They recognize the responsibility of the individual motor vehicle operator as the prime causative factor in accidents. Dr. Harry H. Wagenheim, director of psychosomatic service at Temple University Medical Center, pinpointed this responsibility when he said: "Automobiles don't kill people. Drivers kill people."

Dr. Fletcher D. Woodward of Charlottesville, Va., is Chairman of the A. M. A. Committee on Medical Aspects of Automobile Injuries and Deaths. Vice-chairman is Horace E. Campbell of Denver. Other members are Drs. Jacob Kulowski of St. Joseph, Mo.; Harold M. Brandaleone of New York City; John R. Rodger of Bellaire, Mich.; Seward E. Miller of Ann Arbor, Mich.; James L. Goddard of Washington, D. C.; and Ross McFarland, Ph.D., of Boston. Staff Secretary is Mr. Howard Schulz.

What's Ahead in Mental Health? Conference Is Sounding Board

Can medicine cope with the communicability of certain mental and emotional disorders? What are some of the problems of "learning deficits" in children? Why do mental illness and health in aged persons present a special challenge to medicine? How can physicians and medical students best be trained in psychiatric medicine? What are some problems of the Joint Commission on Mental Illness and Health, and how has it progressed?

Those five broad questions were tackled several weeks ago in separate round-table discussions by 140 representatives of 42 state medical associations and seven national health organizations.* Transcripts of the Fifth Annual Conference sponsored by the American Medical Association and its Council on Mental Health last Nov. 21 and 22 in Chicago now are being compiled. At a banquet in midsession, both A. M. A. President Gunnar Gundersen and Dr. Jonas Salk pointed out the similarity of certain aspects of physical and mental disorders.

Dr. Salk, who is professor of experimental medicine and director of the Virus Research Laboratory at the University of Pittsburgh, cited analogies between the personal immunity to physical disease and that developed against mental illness. Dr. Gundersen told the participants: "Tuberculosis, along with many other diseases, is not related to a single causative agent. It, as well as mental and emotional illness, seems to be multifactorial in the sense that social factors enter into the causation of both." Earlier, Dr. Salk said:

> The idea of communicability of mental and emotional illness requires now a recasting of the concept of causation, etiologic factors, and pathogenesis. A fresh examination from the purely biological viewpoint would be most helpful. Is not the plasticity of the individual during his developmental period the heart of the matter? When the individual has got beyond a certain point in development, he no longer is susceptible to this particular malady, but he may be susceptible to another, whether it is Orson Welles fantasy or something that happens on television for a child audience. The individual is still growing, still changing. All that he is, is not determined by his genes but by a number of events that occur after birth. Why cannot we visualize this as a dynamic situation where there are different degrees of sensitivity or susceptibility or sensibility to different stimuli or different events at different points from the moment of conception to the moment of death?

Following are other summary excerpts from the conference:

Problems of Learning Deficits in Children.—"Isolationism is a relatively uncommon situation, but frequent enough to demand of the physician that he look into absolute rejection by parents. On file is the interesting case of isolationism in a child who had an IQ of 52 at the hospital where he was studied, and with good care and training he showed two years of mental growth in three months. Frequently parents get the feeling that their child is not developing normally, mentally. They do not know where to get help. There are as yet many untrained people in the field. There are not enough psychiatrists in the general population, and only about 200 child psychiatrists who are qualified in the U. S. As a result the burden is placed on the general practitioner. Most often the teacher is the first to find the difficulty but there is a danger that by the time the child who has a mental deficit gets into school the damage might be irreversible. . . . Reading deficits need a great deal of study. Much is known today about reading disabilities and it is tragic when the child who has a reading disability is diagnosed as mentally retarded. . . . Schools for retarded children should not be for adults. There is need for separation of delinquent and aggressive defectives from the child who can be trained."

Education for Psychiatric Medicine.—"Preceptorship training is, by far, the best way to teach psychiatric principles. . . . Medical students seem to learn the didactic or scientific aspects of psychiatry while retaining their cultural prejudices. Influencing such a student with good psychiatric principles could begin at the grade school level and become increasingly important in his premedical education. It is difficult to describe the kind of person who would do best in psychiatry or utilize psychiatric principles in the general practice of medicine. The most common phrase to describe him is that he 'must like people.' . . . What makes a good physician has not been well conceptualized. Admission committees seem to select students on the basis of whether they will pass in medical school and not on the basis of whether they will be good physicians."

Progress and Problems of the Joint Commission on Mental Illness and Health.—The effects of iproniazid and electroshock were discussed as examples of areas of study that should be undertaken. "The Joint Commission should plan projects that are concerned with research in relation to patients' care and what happens to patients after

*The American Hospital Association, American Medical Association, American Psychiatric Association, American Psychoanalytic Association, Council of State Governments, Joint Commission on Mental Illness and Health, and National Committee Against Mental Illness.

Dr. Leo H. Bartemeier of Baltimore is Chairman of the A. M. A. Council on Mental Health. Other members are Drs. Lauren H. Smith of Philadelphia, Vice-chairman; Walter H. Baer of Peoria, Ill.; Norman Q. Brill of Los Angeles; Hugh T. Carmichael of Chicago; Hamilton Ford of Galveston, Tex.; Francis M. Forster of Madison, Wis.; George E. Gardner of Boston; and M. Ralph Kaufman of New York City. Dr. Richard J. Plunkett is Staff Secretary.

psychotherapy. If the Commission is to be extended, more psychiatrically trained doctors should be obtained." There was much discussion of the idea of practicing psychiatrists' engaging in projects within the area of their practice, pooling their information two or three times a year, and then making their reports to the Joint Commission.

(The Joint Commission on Mental Illness and Health is a research and educational organization founded in 1955 by the American Psychiatric Association and the A. M. A. with the cooperation of several dozen other groups to study resources available for the detection, treatment, and rehabilitation of the mentally ill.)

Mental Illness and Health in the Aged.—"We cannot at this time elaborate the problems of housing and the senior citizen, or the economic factors that include insurance and pension plans. Often the economic factors are secondary to emotional needs. There is need to consider whether social values can be changed to make old age an honorable state. Too much premium has been placed on the cult of youth and beauty. There is need to encourage children to feel a sense of responsibility toward aging parents. . . . There is considerable clinical evidence to show that good medical treatment can get 25% of the mental hospital patients over the age of 65 back into the community, and as high as 70% of depressions of old age sufficiently relieved so that they can resume normal living. . . . Whenever possible, the old person should be maintained in his own home. . . . An active and productive life is a protection against emotional decomposition in old age."

Communicability

The conference participants gave special attention—both in a separate round table session and in general discussion—to the relatively unexplored concept of the communicability of mental and emotional illness and health. A summary report stated:

> This concept was a relatively new and provocative one which stimulated a wide variety of thinking within the group, ranging from a description of outstanding examples of "epidemics" of emotional disturbance—such as the panic resulting from Orson Welles' radio broadcast [in 1938, depicting realistically in news format an attack by invaders from another planet], panty raids in colleges, and certain types of religious revivals clearly related to environmental factors—to individual personal experiences with emotional disturbance arising out of distorted thoughts, feelings, and attitudes transmitted between family members. The concept of communicability of mental health is a concept of equal importance with that of communicability of mental disorder.

As participants warmed to the subject, they voiced provocative ideas such as the following:

"It seems a substantial number of patients become mentally disturbed by talks with their doctors."

"The kind of communicability that exists in mental illness is much greater than in measles or other similar diseases."

"In the field of neuroses, anxiety-ridden parents or teachers may evoke anxiety reactions in their children or pupils. Poor leadership with subsequent defective morals prepares the groundwork for a

Selected Quotes from A.M.A.'s Annual Mental Health Conference

ON OLD PEOPLE—

Many of the people who reach old age become a problem because they are isolates. They have no families on whom they can rely. . . . Family relationships frequently are stressful, and some of the problems of old age are the expressions of some of that stress.
—Discussion on "Mental Illness and Health in the Aged."

Too often when we follow the urge to rid ourselves of a burden like old people, we send them to a hospital. And I tell you, when that happens, the old life is shortened. Maybe we as physicians should stand up and not too easily agree with families that want to hospitalize their elders.
—Dr. Leo H. Bartemeier, Chairman, Council on Mental Health.

ON CHILDREN—

The more that psychiatrists can contribute to the diagnostic field, the greater chances there will be that many children who are presently diagnosed as feeble-minded, mentally-retarded, etc., will not fall into this category. . . . Many are not in this category at all.
—Discussion on "The Problems of Learning Deficits in Children."

ON COMMUNICATING THE ILLNESS—

The concept of the communicability of mental disorder should be accorded all possible consideration in research planning. . . . Efforts directed toward training psychiatrists in this important field should be commended. . . . Psychiatrists do not now generally have the epidemiological orientation required for the development of a conceptual framework for epidemiological study of mental disorder.
—Discussion on "Communicability of Mental and Emotional Illness."

In years past, nostalgically speaking, the public health and epidemiological approach to specific disease

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high incidence of emotional illness which is communicated."

"Since the word 'communicability' has had a specific medical sense for centuries, are we justified in giving this word an enlarged meaning? It would be ridiculous to try to defend the assertion that all mental disorders are communicable."

"The epidemiology of healthy ideas and healthy behavior is an epidemiology of the future."

"I suspect there is a very direct correlation between the general level of emotional maturity in individual members of a given culture and the decline of that culture. What are the socioeconomic and governmental factors which prevent the maturation capability in our citizens? Medicine as a whole should spend a lot of time thinking about this and talking about it. This is an excellent opportunity for organized medicine to get together with the sociologists, the historians, the law enforcement representatives, and others—to lead our country's cultural development instead of following it. Educators are as alarmed as we physicians are at the 'cultural deterioration,' the need for improvement."

"During the Hitler regime paranoia became not merely an epidemic, but a national policy by one man, against whom large masses of population apparently were unable to immunize themselves."

"In epidemiology, mental disorder has got to develop on a conceptual framework of psychiatry. General epidemiologists can contribute method, but it will never be epidemiology of mental disorders unless you get psychiatrists who are trained in epidemiological methods, and that is one of the critical things we need."

Does She Drive Him to Drink? Plan Aids to Wives of Alcoholics

"The wife is often a critical link in the rehabilitation of an alcoholic husband. She can help him, or she may, without intent, almost literally drive him to drink." Based on this theory, the Chicago Committee on Alcoholism this month announced plans for new group and individual services for wives.

The committee recently spent several months offering such services on an experimental basis, and the experiment was considered successful.

Dr. Patrick Israel, psychiatrist and phychiatric director of the committee, said sessions will be held periodically for wives who feel that their husbands have an alcoholism problem. He said: "They will be given information about the illness of alcoholism and suggestions as to the kind of behavior on the part of the wife which is likely to be most helpful for living with the problem and in getting the husband to understand his own need for obtaining assistance in overcoming his alcoholic pattern."

The committee, which operates Portal House, an outpatient clinic for the treatment of alcoholics, is concerned with education, research, and treatment in the field of alcoholism (see Medicine at Work, THE JOURNAL, July 19, 1958).

problems now would seem to have been fantastically simple, compared to our present problems in mental illness. . . . We face in essence a heretofore unrecognized epidemic throughout our country and the world.
—Dr. Gunnar Gundersen, President of the A.M.A.

The cells that produce polio are conditioned to respond when a virus threatens the body. . . . There is no reason to believe that cells of the nervous system will not respond in the same way as cells that create the immunity to polio. We are really concerned with the problem of biology as it relates to many fields.
—Dr. Jonas Salk, University of Pittsburgh School of Medicine.

ON COMMUNICATING THE PROBLEM—

We psychiatrists are not always effectively communicating with our colleagues in medicine. Not enough of us are leaving our ivory towers. No wonder some physicians refer patients to psychologists—instead of to psychiatrists—for psychotherapy. They don't know the differences between psychologists, psychiatrists and psychoanalysts. Because they don't know, they fear—and because they fear, they tend to fight the good that we, who also are in medicine, are trying to do. —Dr. Alfred Auerback, San Francisco psychiatrist.

Mental health committees [of medical societies] can help educate the governing bodies and the officers of their state medical associations. Furthermore, they can be a great deal of help in education, often by meeting with prominent non-physicians in the state. —Discussion on "Education for Psychiatric Medicine."

ON INTERNATIONAL COMPARISONS—

The Joint Commission on Mental Illness and Health should make comparative studies between the United States and other countries with regard to methods, procedures and research on various projects. . . . Various countries of the world have different standards of procedure and definition in evaluating mental illness and health. —Discussion on "The Joint Commission—Progress and Problems."

Survey of Small Plant Occupational Health Programs

Hundreds of small business firms have success stories to tell about their occupational health programs, and the A. M. A. wants to relay those stories to physicians everywhere. To do this, a survey of the various types of medical services provided by physicians in charge of such programs will be made this year by a committee of the Councils on Medical Service and Industrial Health.

The survey will also seek to determine the various arrangements through which these services are provided in the plants employing 500 and fewer workers. Case studies for each program will cover such points as location of establishment, type of industry, types of medical service provided, arrangements and administrative procedures used, origin and objectives of the program, hours of service provided, description of the occupational environment, and relationships between the physician serving the program and other physicians in the community.

Physicians in individual private practice, in clinics, or in various other arrangements through which occupational health services are provided to small plants who would like to take part in the study are invited to communicate with the Committee on Medical Care for Industrial Workers, 535 N. Dearborn St., Chicago 10, for additional details. The committee believes that publication of the case studies will help other physicians and management who are interested in developing such programs where they do not now exist or in evaluating those programs presently in operation.

Can Discoveries Be Coaxed?

Names prominent in pharmacology, research, biochemistry, medical journalism, clinical science, and industrial technology figured on the program of the world's first serendipity ("happy accident") conference which ended two weeks of session today at Nassau, Bahamas.

As "animateurs," they stimulated free discussion among representatives from various disciplines on the role of serendipity (see Medicine at Work, THE JOURNAL, Dec. 21, 1958) in such fields as chemical synthesis, endocrinology, organic disease, enzymology, and neurology. Dr. B. L. Frank of Montreal, who organized this First Bahamas Serendipity Conference, said:

"From the start, our goal has been to break down the barriers between specialized fields and to encourage the cross-fertilization of ideas which might lead to unforeseen results. Perhaps, this way, serendipity can be controlled to the point of coaxing discoveries or inventions—finding something accidentally on purpose."

Each discussion lasted two hours for all participants. Smaller and more informal groups then carried the theme further. Among "animateurs" on the conference program were:

Dr. R. Keith Cannan, chairman, division of medical sciences, National Academy of Sciences.

Dr. Alfred Gilman, professor of pharmacology, Albert Einstein College of Medicine.

Dr. Henry B. Hass, president, Sugar Research Foundation.

Dr. Edward C. Kendall, award-winning biochemist, Princeton University.

Dr. I. Arthur Mirsky, professor of clinical science, University of Pittsburgh School of Medicine.

Bernard E. Schaar, president, Schaar and Company, scientific apparatus.

Dr. Abraham White, associate dean and professor of biochemistry, Albert Einstein College of Medicine.

Dr. Walter F. Riker, professor of pharmacology, Cornell University Medical College.

Dr. Austin E. Smith, former editor, THE JOURNAL.

Tax Deferred Savings—One Way To Pay for Medical Care in Old Age?

If Poor Richard never said "Save for your old age," it's probably only because he didn't think of it. It's the kind of eye-to-the-future thrift that appealed to him.

To encourage just this kind of thriftiness, Frank Dickinson, Ph.D., last month advocated federal legislation allowing workers to salt away up to $100 per year, tax deferred, to pay exclusively for medical needs in old age.

His suggestion came, coincidentally, just as the National Association of Insurance Commissioners approved a change—the first in 17 years—in the mortality table, a statistical record of the rates of death at different ages. "Life expectancy," they said, "has reflected an explosive increase."

Dickinson, who recently retired as head of the A. M. A.'s Bureau of Economic Research, offered his idea Dec. 28 in a paper presented at the American Association of University Teachers of Insurance meeting in Chicago.

Under this plan, any worker would be allowed to put aside up to $100 a year in a special private account. His taxable income for that year would then be reduced by the amount of the deposit. On retirement, the accumulated savings in the special account could be used to meet medical and hospital bills, purchase health insurance, or buy a medical and hospital care annuity. Payment of tax on the money would be made as it was withdrawn.

General Practice and Worker Health

Although the annual Congress on Industrial Health in Cincinnati next month is expected to attract chiefly industrial doctors, it should be of interest to other physicians, too. This is because general practitioners are the ones who provide occupational services for most workers; three-fourths of the nation's labor force is employed in firms not

having industrial physicians (see Medicine at Work, THE JOURNAL, March 30, 1957).

The Congress, sponsored by the A. M. A. Council on Industrial Health, will be held Feb. 16 through 18 in the Netherland-Hilton Hotel. To be included are:

—A panel discussion of industrial health education at all levels.

—Papers on such research problems as noise, radiation, cancer, and toxicology.

—Reports on cases of industrial disease presented by fellows and staff of the University of Cincinnati Institute of Industrial Health.

Another A. M. A. Meeting Soon

Kansas will be the scene of the 14th National Conference on Rural Health to be held in Wichita March 5 through 7. "Horizons in Rural Health" is the theme of the meeting sponsored by the A. M. A. Council on Rural Health, together with state medical societies and farm, educational, and allied organizations.

Spread 'Homemaker' Idea

Where does a family go for aid when the mother is hospitalized or incapacitated, the father must work, and there are no relatives to help out? In 150 U. S. counties, the obvious answer is "to a homemaker service."

To increase the number of counties in which such an answer is possible is one of the main objectives of the National Conference on Homemaker Services to be held Feb. 10-11 at the Edgewater Beach Hotel in Chicago. Sponsors, in addition to the A. M. A., include 25 voluntary and governmental organizations.

Preconference study groups have prepared 12 working papers which will form the basis for conference talks. One development to be discussed is the sponsorship of a homemaker service by the Passaic County (N. J.) Medical Society and its Woman's Auxiliary.

Information on registration for the conference may be had by writing to the Council on Medical Service, American Medical Association, 535 N. Dearborn St., Chicago 10.

Big City Experiment for AMEF

A five-minute period at the beginning of all departmental meetings held in Minneapolis hospitals in November was used to promote contributions to the American Medical Education Foundation.

Dr. Harold G. Benjamin, AMEF chairman for the Hennepin County Medical Society, said the method was an experiment in solving a major solicitation problem: complete coverage of a large city's physician population. This month the medical society pronounced the experiment a success.

The Moon Is Old Hat

Medicine, Other Sciences Explore Space Frontier

Milton Golin

The Time: Veterans Day, Nov. 11, 1958.

The Occasion: Second International Symposium on the Physics and Medicine of Atmosphere and Space.

The Participants: Hundreds of physicians and other scientists interested in the problems of space conquest.

The Place: San Antonio, the Hilton Hotel—near the scenes of other conquests 112 years ago, when Texans fought the early battles which led to U. S. acquisition of the entire territory west of the Mississippi.

That was the setting near the hallowed bones of Crockett, Bowie, and Travis—pioneers in their own right. But how different were the pioneers of 1958 as they looked toward the decades ahead!

—Sipping soft drinks, they cast unsmiling, sophisticated glances at the lobby sign which read: "Make your next symposium at the Lunar Hilton—1960."

—Elbowing their way through the jammed auditorium doorway as loudspeakers carried program remarks to the adjoining foyer, some of them muttered about lack of space at the space symposium. (The Air Force and the Southwest Research Institute had figured on only 500 participants and a handful of newsmen when they planned the meeting. Nearly 800 showed up, including 73 reporters.)

—Seated comfortably inside, others were regarding moon-region flights as "old hat." Their thoughts were beyond—as they listened to papers on speed-of-light propulsion, closed ecologic systems, problems of rescue in space, the physical environment of Mars.

The forward tone was sounded by James A. Van Allen, Ph.D., head of the department of Physics at the State University of Iowa, when he said: "We would like to emphasize interplanetary or space probes rather than merely moon shoots." Another physicist said: "We have cracked the scientific problem for orbital or lunar flight. It is up to the technologists to follow through. We are concentrating realistically now on probing Mars and Venus."

But what about the medical problems—how close are they to solution? A good many physicians, some of them active in keeping the American Medical Association up to date on such matters, assembled around the time of the symposium to absorb a sort of postgraduate refresher course. They included Dr. Jan Tillisch, Chairman of the A. M. A. Committee on Aviation Medicine which met on the eve of the symposium; Dr. B. Dixon Holland, Staff Secretary of the Committee and its parent Council on Industrial Health; Navy Capt. Oran W. Chennault,

M.D., another Committee member; Dr. William J. Kennard, then acting director of the A. M. A. Washington office and an aviation medicine pioneer in his own right; Dr. Richard Meiling, a member of A. M. A. Board of Trustees ad hoc committee concerned with aeronautics and space; Dr. Harold Lueth and Mr. Frank W. Barton, another member and Staff Secretary, respectively, of the ad hoc committee; Dr. Carroll P. Hungate, a member of the A. M. A. Council on National Defense; and the Associate Editor of THE JOURNAL.

A physician even more closely concerned with the health aspects of space flight, Major Gen. Otis O. Benson Jr., commandant of the School of Aviation Medicine at Randolph Air Force Base near San Antonio, told the symposium: "The fact that we have to deal with a multitude of environmental factors shows, more than ever before in the history of human progress, a very close cooperation between physics and engineering on the one hand, and medicine and biology on the other."

Progress of Decade

Next month (on Feb. 9) the School of Aviation Medicine will observe the 10th anniversary of the founding of its space medicine department. Much has happened in the decade since a physician, an astrophysicist, and a bioclimatologist launched operations of the department (see Medicine at Work, THE JOURNAL, June 15, 1957). "Space medicine is a logical extension, is an approved and accredited specialty ranking with the time-honored divisions of medicine," said General Benson. "Now the School of Aviation Medicine has on its staff scientists trained in medicine, space medicine, biology, botany, psychology, biometrics, mathematics, electronics, biophysics, radiobiology, microbiology, astrophysics, and engineering. We also have a number of skilled pilots, many who have scientific training."

One such man is designer-engineer-test pilot A. Scott Crossfield of North American Aviation, Inc., who spoke at the symposium. This month, in a rocket-powered X-15, he was scheduled to be the first man to fly an airplane designed to journey weightlessly (for him) into space 100 miles or more above earth. He said: "Aeromedical problems in orbit are—in order of importance—boredom, zero g [weightlessness], radiation, and then some of the difficulties of detachment. The boredom thing is serious. It is nature that a pilot literally goes to sleep at the switch when he has nothing to do. Demanding tasks enhance his entire performance."

Following are other medically oriented comments from symposium participants:

ON WEIGHTLESSNESS—

There is now a statistically, significantly founded basis for the assumption that man can handle the zero gravity situation for short periods of time. The final answer concerning longer periods, however, can only be found in a manned orbiting vehicle. It is up to the ingenuity of the engineer to invent magnetic and other kinds of devices which may provide a make-believe gravity.

—Hubertus Strughold, M.D., professor of space medicine (see interview in this section of THE JOURNAL).

We are concerned that when the weightless state becomes longer there may develop minor physiologic disturbances which, if cumulative or irritating, may cause or enhance psychiatric symptoms. We can best investigate this by utilizing our rocket capabilities to establish biological laboratories in the sky.

—Siegfried J. Gerathewohl, Ph.D., research psychologist for Army Ballistics Missile Agency.

ON RADIATION—

The cosmic ray measurements of our space satellites and probes have brought about a revolutionary change in the basic concept of the extra-atmospheric radiation field. . . . A radiation intensity prevails which would administer a lethal dosage in a few hours' exposure.

—Herman J. Schaefer, Ph.D., research scientist in radiation biophysics at U. S. Naval School of Aviation Medicine.

ON DETACHMENT—

Exposure to "everyday life" in space over a period of one to several weeks, or even months, in an orbital test bed is an important factor in conditioning a space crew for prolonged absence from earth.

—Krafft A. Ehricke, assistant to the chief engineer at Convair-Astronautics.

ON STRESS—

Studies at this time indicate that man is adaptable, enduring and strong enough to withstand the stresses anticipated, and through the use of sealed cabins, he can be indoctrinated and trained to acceptable performance levels.

—Lieut. Col. George R. Steinkamp, chief of the Department of Astroecology at Air Force School of Aviation Medicine.

ON NUTRITION—

The yeast cycle is being considered to provide a method for stabilizing human waste products by means of bacteria and to make the waste available as appropriate food for both algae and the yeast. Whether a large quantity of yeast could be eaten to operate this cycle over long periods is not known. . . . The interposition of an animal such as a goat, a daphnia, a slug, a snail, or some other animal which is likely to eat algae directly would yield animal protein for the space crew.

—Robert G. Tischer, Ph.D., head of the Department of Bacteriology at Mississippi State University.

During a weightless state, a certain danger exists when attempting to drink from an open container. The liquid tends to disperse upon contact with the lips, and to slip into the sinuses and the respiratory tract. The danger of aspiration is real. Sucking or squeezing the liquid from a bottle solves this problem.

—Siegfried J. Gerathewohl.

ON HEALTH HAZARDS GENERALLY—

Man has not had to cope with the following unknowns he will encounter during our initial space flights: Extended periods of weightlessness, extended periods of isolation

and/or confinement, eating and sleeping and working and accomplishing normal body functions under hostile environmental conditions, high accelerations and decelerations, high temperature, low pressure and radiation. . . . And yet, these problems are not insurmountable. A capsule can be built within the weight limitations of our available propulsive capability, thus allowing us to achieve manned space flight soon.

—Major Gen. Bernard A. Schreiver, commander of the Ballistics Missile Division, Air Research and Development Command.

How soon will the U. S. achieve manned space flight? Sooner than many people believe, according to the journal, *Missiles and Rockets*. It reports that a joint military-industry program—complete with formal specifications—is now under way for construction of a 2,000-pound manned satellite capsule that would replace the nose cone of a standard Atlas intercontinental missile to be launched from Cape Canaveral, Fla. Several dozen contractors were supposed to submit bids on the project last month, with trial launchings (first with dummy payloads and then with small animals) expected soon after construction begins this year. Already, the Air Force is laying plans to send a number of two-pound monkeys separately into orbit by the middle of this year, according to Brig. Gen. Donald D. Flickinger, director of life sciences for the Air Research and Development Command.

Words, Actions, Trends

Those are the words, actions, and plans which portray the rocketing rise of space medicine as physicians join with other scientists in an upward-look-with-feet-on-ground. There will be more space medicine symposiums—like the one at San Antonio—and at the regional level, too, like the ones sponsored by medical educators in Santa Monica, Calif., last Oct. 22, by the Bexar County Medical Society in Texas the same month, and by the San Mateo County (Calif.) Medical Society last September.

There will be greater interest at top federal levels, as policymakers—selecting a civil air surgeon—consider his qualifications to attack both physiological and psychological problems involving high-speed jet and rocket flight. And there will be world-wide concern, too, as 15 nations (including the U. S. and the U. S. S. R.) assign nonpolitical representatives to the new international committee to coordinate space research (COSPAR) later this year.

The race for space supremacy is so intense, and yet so broadly attractive, that even amid tight secrecy within individual nations, statesmen call for letting down the bars. One side of that paradox is personified by the FBI agents who kept a constant watch on an uninvited Polish biologist who had "crashed" the symposium at San Antonio. The other side is heard in the words of U. S. Senator Lyndon Johnson at the same meeting: "In a world circled by vehicles of space, there can be no secrets. We need, therefore, to concern ourselves not with guarding what we know but, rather, with exchanging and pooling our knowledge with all the community of free men. . . . The space frontier is, above all, a perpetual frontier."

Medicine has become a partner with other sciences in the exploration of that frontier—and the profession may expect research rewards that can benefit the man on the ground as well as the man in outer space. The former Air Force surgeon general, Dan Ogle, has pointed out that techniques in miniaturizing and otherwise refining instruments for recording animal reactions aloft is hastening the improvement of many professional appliances in terrestrial diagnostic procedures for humans. He says: "Maybe these new devices will help save the life of an Ozark woman whose hill doctor was stumped."

General Flickinger believes that the study of mice catapulted into radiation zones may one day furnish leads for cancer research. Other physicians foresee a variety of untold benefits accruing from space findings directly to earth application. Dr. Hubertus Strughold expresses the point this way:

"The extension of medical research into the extraterrestrial realm of space will not only promote man's conquest of space, it will also broaden our knowledge in medicine and biology in general and, therefore, will be of general benefit to mankind."

Three scientists chat informally at symposium on space medicine and physics in San Antonio. *Left to right*, Wernher Von Braun, Ph.D., technical director of the Army Ballistic Missile Agency at Huntsville, Ala.; Hubertus Strughold, M.D., professor of space medicine at Randolph Air Force Base, Texas; and L. R. Shepherd, Ph.D., chairman of the Council of the British Interplanetary Society.

—Leslie W. Bland photo

Interview with Pioneeer "Space Doctor"

Medicine Ready to Keep Man Alive in Trip Up, Around, Down

How far has medical research moved toward safeguarding the health of the first man in orbit? What are some of the human problems of space flight? How does space medicine interrelate with the profession generally, with medical education, with allied sciences and technologies, with industries making space vehicles?

Dr. Hubertus Strughold, often called "the father of space medicine," answers these and other questions in the following wire-recorded interview with THE JOURNAL *at San Antonio, Texas, where 700 physicians and other scientists assembled several weeks ago for a symposium on the physics and medicine of atmosphere and space. Dr. Strughold was director of the Aeromedical Research Institute in Berlin before World War II. Now he is an American citizen serving as advisor for research and professor of space medicine at the School of Aviation Medicine, Randolph Air Force Base, Texas.*

Q With commercial jet aircraft now carrying humans at 35,000 ft., what kind of health dangers exist to passengers and crew?

A One danger is explosive decompression—the plane suddenly losing air pressure to the 35,000-ft. level from the comfortable cabin level of 8,000. There are measures for coping with this problem. At that altitude there are no dangers to passengers from any increased cosmic radiation. There is, however, one significant problem which arises after the flight—disruption of the normal day-night cycle.

Q Would you explain that?

A Today, it takes a propeller-driven plane about 12 hours to cross the Atlantic. In a few months, when jet airliners will begin dominating the ocean sky, it will take only six hours as the aircraft whizzes past six or seven time zones. Let us say that a passenger lands in New York at 3 p. m., when it is 9 in the evening in Europe. His appetite is thrown out of kilter. He is very sleepy and may doze off, awakening at 3 the next morning.

Q So this corresponds to sleeping and eating problems of a night worker?

A Yes, more or less, with some complexities added. Say a businessman has a very important meeting in England. Because of the upset day-night cycle he arrives unprepared, psychologically, for his work. So he should plan on arriving a few days before the meeting.

Q How does this concern the physician in practice?

A It is something he should reckon with in patients who make long overseas flights. And there is another point. Body temperature normally reaches a high around 5 in the afternoon. Suppose a man flies to New York from Paris while he has a cold, or perhaps another kind of infection. His physician finds an unusual temperature at 11 a. m. New York time when it may not be unusual at all.

Q How would space flight intensify the day-night cycle problem?

A In space travel there is no day or night. A vehicle in orbit would be 20 minutes or so in the shadow of the earth, perhaps 60 or 70 minutes in the sun's rays. So we must provide submarine conditions in creating an artificial day-night cycle.

Q What kind of submarine conditions?

A Setting periods for duty, recreation, and sleep. Submarine crews change duty every four hours, and this might be best for space crews, too. We are experimenting.

Q If technicological problems can be solved, when will we be ready—from the medical standpoint—to keep a man alive from the time of launching, through several days of orbiting, and during reentry into the atmosphere and recovery?

A We are ready now—if we can solve the recently defined problem of radiation. There are certain ways to get around that problem. One might be to launch into a route over the polar region, where it appears the radiation belt narrows. Or the vehicle velocity might be increased to shorten the time of exposure. This problem will occupy us for the next year.

Q In an interview two years ago you predicted that by the 1960's we would see 25-minute coast-to-coast flights by rocket ships looping through space. What is your estimate now?

A The same. But I was misquoted then. I said 45 minutes, not 25.

Q In the spring of 1957, before sputnik, you told THE JOURNAL [see Medicine at Work, June 15, 1957] about the space cabin simulator which nearly duplicates extraterrestrial conditions. How has that kind of study progressed?

A We now have greater knowledge of air regeneration, of carbon dioxide elimination, of the human effects of hibernation, and of the day-night cycle. So far, a man has spent seven days in the simulator. That would cover a trip to the moon. Experiments are still going on, relating to other conditions and to applications that I cannot speak about at this time. I can say, however, that we will have a space cabin simulator for two men when the special building for space medicine is completed at Brooks Air Force Base next July.

Q How might research in space medicine benefit the profession and the general public along specific medical lines—such as nutrition, psychiatry, orthopedics, physiology, pharmacology, ophthalmology, cardiology? How might physicians, generally, help solve some space medicine problems?

A A very interesting question. We will never achieve success in space flight without the vast knowledge of medicine through the ages. For example, physicians have a much better idea now about radiation than they had 5 or 10 years ago. Of course this is important in solving health problems

in space flight. At the same time, the science of physiology is benefited by what we in space medicine are learning about weightlessness. And that point on cardiology—in weightlessness, we find that blood circulation is not affected very much. This is very important.

Q Do chewing, drinking, digestion, and elimination of body wastes function at zero gravity?

A With proper preparation, yes. As far as we can learn they do work—at least for short periods of time. We have reproduced weightlessness for no more than one minute for a human.

Q Are there any efforts to exchange space medicine data with Soviet physicians?

A No specific channels. They translate every paper on space medicine in the U. S.

Q How do the two countries compare in space medicine knowledge?

A The Soviets work in this field at the Institute of Aviation in Moscow and, it seems to me, at some other place. My general idea is that they are not ahead in this field—actually, they have been inspired by some events here in the United States—for example, when we rocketed monkeys into space.

Q Is there any reason to believe that the Soviets might more likely risk a man's life in order to launch him into space before we do?

A In my opinion, yes. But I also have the impression from reading the Russian medical literature, and from recent scientific conversations in Amsterdam, that they plan especially to get a dog into orbit and get the animal back.

Q What do you consider the optimum physical, mental, and emotional characteristics of the so-called premium space man?

A First let me say what I do not consider optimum—not a hermit, not a monk, not a schizophrenic. We also hear that a woman should be first in space, which would be nice and also very cavalier. But you would have to train a woman 10 years for that task. From a medical standpoint an experienced jet pilot should be first in space.

Q What other prime characteristics would be necessary?

A Motivation. He would have to want to go. He would also need to know something about the nature of space. And he would have to be familiar with medical problems in flight.

Q Would he need a personality to adapt to aloneness, or would he need to be conditioned to the problem of, as one speaker here described it, "developing an effective umbilical cord" for himself outside the earth's influence?

A I think both factors operate.

Q A little while ago you said that, from the medical standpoint, we are able to send a man up and keep him alive and well through return. Now we hear of algae as the key to a closed-cycle feeding system that will keep him nourished. How critical is this closed-cycle feeding problem?

A I don't feel that we must achieve such a system for an initial flight of, say, up to six weeks. Food can be brought along.

Q What about water?

A We have recently learned that 10% of a man's own water—called metabolic water—can be recovered daily. We can refine potable water from urine by a process that is relatively simple in a space cabin simulator. So it is not necessary to take too much water along.

Q In your experience, what manpower needs exist for the space-oriented physician as a part-time or full-time consultant in the aircraft industry?

A There is a demand for physicians of that training. Four or five years ago space medicine was a tiny part of the Air Force School of Aviation Medicine. Now almost every big company has a physician to study human factors in space flight. Convair has a physician for aeronautics and another for study of human factors.

Q Where would a physician interested in space medicine get his training?

A At the present time at Randolph, the Aeromedical Laboratory at Wright Field, or at Ohio State University. I do not believe that medical schools should establish courses in space medicine, although they might integrate the subject into the total curriculum—just as, 20 years ago, medical schools started to include lectures on aviation medicine. I think the whole field of medicine could be made much more interesting by including some phases of space medicine. The study of physiology, for example, could become really exciting if there were just a one-hour lecture on the effects of weightlessness on various body actions.

Q At this conference, participants included—besides physicians—astronomers, physicists, chemists, biologists, and representatives of other fields. Is it an advantage or a disadvantage when men of diverse disciplines meet to tackle a single problem such as space flight?

A A great advantage, definitely. In fact, this is the first time that we have had a medical meeting where at least half of the participants are not medical doctors. They are learning something from us, and we learn from them. Each is knowing where the other is trying to go.

Q What would you think is the next area for exploration involving physicians and other scientists at a future space symposium?

A Probably the same problem area as now. There might be some new problems, too, though—like antimatter, a point in physics. Time adaptation also should be discussed on a broader basis. But basically we in medicine are not so much concerned with distance as we are in duration of space flight. Our task is to develop more effective mechanisms to make longer and longer space exploration. We cannot determine the timetable. That is for the technologists and the rocket engineers.

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REPORT OF JOINT COMMITTEE ON THE NARCOTIC PROBLEM

A JOINT Committee of the American Bar Association and the American Medical Association has been engaged in a study of the narcotic problem for the past three years. Research has been conducted to ascertain the extent of this problem in those European countries equal to the United States in industrial development and to study the legal structure which these countries have erected to combat it. The present status of the narcotic problem in the United States was reviewed, and certain recommendations for further studies, both legal and medical, were made. The first report is a mine of information about the problem, and it contains much of great interest to doctors.

The situation in Europe differs from that in the United States in at least three ways: the number of known addicts is much smaller than in the United States, so the problem is far less acute; the penalties provided for persons convicted of violation of the narcotic laws are far less severe than those provided by our recent laws; there is more disposition on the part of the legal authorities to regard the problem as a primarily medical one and to turn a larger proportion of it over to the doctors.

Whether the severity of our laws is a factor aggravating or ameliorating the problem in the United States is debatable, but the question is likely to be settled by the passage of time, for Congress has recently made the laws still more severe. Certain members of the judiciary, as the Committee is advised, feel strongly that the penalties prescribed by the laws are unduly severe and that they do not have a proper relation with the penalties for other criminal offences. The mandatory sentences which these judges are required by law to pronounce are often at variance with their sense of justice, but any plan to turn over the problem to the medical profession raises the question how well this profession is prepared to deal with it. Certainly the tendency in recent years has been to increase the scope of medical efforts; for example, those suffering from undue anxiety, a subject of great interest to all doctors today, a generation ago were thought not worthy of the attention of the profession. One wonders how many physicians practicing today would welcome patients with problems concerned with addiction into their offices, or have any good idea of how to help them.

We need not accuse ourselves of lack of progress. The U. S. Public Health Service narcotic addiction hospitals at Lexington and Fort Worth are without doubt the best of their kind in the world and the research being conducted there is world-famous. We know how to withdraw addicts from their drug with safety, and we are making progress in lessening the discomforts of withdrawal, but we need to study methods of prevention. This and many other problems, such as that of relapse, cannot be successfully attacked from institutions such as Lexington and Fort Worth, where patients are seen only after they have become addicted.

To the Joint Committee it seemed obvious that the next step was to establish an experimental outpatient clinic in an urban center where addiction is prevalent, such as Washington, D. C. Such a clinic could be primarily charged with the supervision and help of former addicts discharged after withdrawal, and with patients referred to it by the courts, but this might prove to be but a small part of its activities. When it is noised abroad that there is a place to which those confronted with problems related to addiction can go for understanding and help, many may resort to it voluntarily and, if it is successful in developing practical methods, doctors would have the advantage of this experience in the handling of their own patients.

The development of a program for the intensive postinstitutional treatment of addicts has already been advocated by the Council on Mental Health of the A. M. A., and the Joint A. B. A.-A. M. A. Committee endorsed this view, recommending a limited experiment which could test various ways and means. Such a clinic could determine whether it is possible to rehabilitate addicts in a noninstitutional setting, so that they can live and function without drugs. The disciplines of medicine, psychiatry, psychology, social case work, and education should all be used. The clinic should offer psychotherapeutic guidance in dealing with their personality problems and social work help with family difficulties and vocational guidance. In short, every effort should be directed toward enabling the addict to become productive without drugs.

This may not always be as difficult as some have believed. The medical profession is most conscious of the worst side of the picture. It is the repeaters at Lexington who attract attention and provide

The members of the Joint A. B. A.-A. M. A. Committee on Problems of Narcotic Addiction are Rufus King, Esq., Chairman; Judge Edward J. Dimock; Abe Fortas, Esq.; Dr. Robert H. Felix; Dr. Isaac Starr; and C. Joseph Stetler, Esq.

data for the literature; those who remain off the drug are hard to follow and do not appear in doctors' offices. The resolution of the House of Delegates of the A. M. A. that ambulatory treatment of addiction was impossible was passed about 35 years ago, largely as a result of acute dissatisfaction with a group of doctors making money by supplying addicts with drugs. Studies made on the adolescent addicts in New York indicate that many of them simply decide to give up the habit and do so without medical assistance of any kind. Persons lightly addicted have few withdrawal symptoms. Successful police work is reflected by the great dilution of the drugs now sold in the black market; it is more difficult to become heavily addicted than was formerly the case. Improved methods of minimizing the withdrawal symptoms, as by substituting one of the newer synthetic drugs before withdrawing, are being developed. Perhaps more patients could be successfully treated as outpatients than most now think. Certainly the psychological trauma inherent in confinement in Lexington or some similar institution should be avoided if possible.

The question of what should be done with addicts who persist in their addiction despite the clinic's best efforts leads to a controversial field where strong opinions are many and facts are few. The history of the belief that clinics for the low-cost distribution of drugs to addicts are the solution of the narcotic problem is treated at length in the joint A. B. A.-A. M. A. report. The report is clearly skeptical that any easy solution lies along those lines and agrees with the recommendation of the Council on Mental Health that the A. M. A. should not approve clinics which would dispense drugs to addicts at this time, but, like the Council on Mental Health, they were tempted by the possibility of a limited experiment conducted by experts to shed more light on this important aspect of the problem. It was the opinion of the legal members of the Joint Committee that such a test, if conducted by the experimental clinic, would not violate present laws.

The time, therefore, seems ripe for an extension of the medical attack on the narcotic problem by the establishment of outpatient clinics devoted to the problem in the centers of populations where addiction is prevalent. Indeed an outpatient clinic for addicts has already been started in New York and plans are under discussion in Philadelphia. Outpatient clinics concerned with medical counseling, chiefly for adolescents, are operating in Chicago, Detroit, and Los Angeles. The U. S. P. H. S. is embarking on a large program. One can say with confidence that such efforts seem well worthwhile.

What matter if, because of the peculiar difficulties involved, those in charge of such clinics will need the best virtues of both the doctor and the saint. The medical profession has risen to challenges before.

The Interim Report of the Joint Committee of the American Bar Association and the American Medical Association and Appendix A, "Some Basic Problems in Drug Addiction and Suggestions for Research," may be secured from Grosby Press, 30 Ferry St., New York City, at a price of $4.50.

Judge Morris Ploscowe is Director of the Narcotic Drugs Control Study instituted by the Joint Committee.

This study has been supported by a grant from the Russell Sage Foundation.

NEW AND NONOFFICIAL DRUGS, 1959

Available for the first time in January of the year of publication, the 1959 annual edition of New and Nonofficial Drugs offers practicing physicians a convenient and up-to-date compendium of the views of the A. M. A. Council on Drugs concerning most of the modern drugs in current use. In addition to revision, where necessary, of descriptions of drugs which are retained in the book for a period of 20 years, it includes new monographs that have appeared in the Council's column of THE JOURNAL since the previous edition was published. Monographs for drugs which are no longer commercially available have been deleted. The organization of contents into chapters according to the clinical application or pharmacological action of drugs has been preserved. Thus the new edition provides in cumulative, classified, indexed, and bound form a concise reference to authoritative information on newer drugs. Physicians are urged to avail themselves of the early opportunity to obtain the latest edition of the Council's annual publication by ordering it directly from the publisher, the J. B. Lippincott Company, East Washington Square, Philadelphia 5, Pa. The modest retail price of $3.35 per copy is a small investment indeed for a book which is so carefully compiled and published as an A. M. A. service to the medical profession.

In today's era of "polytherapeutics" (numerous drugs for identical or similar clinical uses) the current edition of such a book as New and Nonofficial Drugs should be almost indispensable, if not a "must," for the practicing physician. Known trade names for all described drugs are listed in conjunction with monographs, and in the index, to facilitate identification of drugs which the Council describes under recognized nonproprietary terminology. Commercially available pharmaceutical preparations, including sizes or strengths of dosage forms, also are listed in conjunction with monographs as an aid to prescribing. Most important of all—the Council's unbiased descriptions of the actions, uses, limitations, hazards, routes of administration, and dosage of drugs should enable physicians to determine their suitability for use in practice. Physicians generally also should be aware that the scope of the publication has been expanded since 1955 to encompass all individually available commercial preparations of drugs, whether or not their clinical usefulness has been established.

Physicians who have never used the Council's annual publication, or are unfamiliar with its modern features, might well consider its annual purchase as a current office guide to drug therapy.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

For some time supporters of a movement to give hospital and medical care to social security beneficiaries have referred to the problem of the aged as primarily an economic one. Only the federal government, they contend, can cope with this large economic problem.

The American Medical Association disagrees with both allegations. Your Association's position is that the problem of senior citizens is basically a broad social one and the solutions to the many enigmas within the over-all problem must be found and implemented at the local level. Furthermore, huge federal spending cannot solve special considerations—social, psychological, physiological, and occupational—that confront our older citizens.

In this nation, perhaps in the entire world, a revolution in aging is taking place. It will affect Americans of all ages and may compare in breadth with the industrial revolution. Therefore, it is extremely important that we find out (1) the primary needs of older citizens, (2) who is responsible for meeting those needs, and (3) when they should be met—before old age or on a catch-as-catch-can basis in the critical years of senior citizenship.

Our entire thinking on the subject of aging and the aged must be as dramatic and forward-looking as the revolution itself. We dare not cling to the old perspective of aging in the face of longer life, better health, and increased productive potential on the part of our senior citizens. If we do, we will deny them and society the rewards for which medicine has fought in its war against disease.

If we separate a substantial part of our population from the rest of the human family through legislative fiat, employment and retirement policies, and community attitudes simply because they have reached a certain chronological age, we will court economic and social disaster. Simultaneously we will create an emotional problem for countless oldsters which tend to make them illness-prone.

Therefore, I believe we must begin now to give all persons—regardless of age—the full opportunity to participate in our nation's life to the extent of their desire and ability. We must eliminate present arbitrary retirement policies and other economic and social barriers to life fulfillment by the aged. We must promote health maintenance programs and wider use of restorative services, remembering that it is more desirable to restore the disabled to activity than to put them on the shelf.

We must continue to insist that adequate indigent medical care programs should be developed at the state and county level and we must reaffirm our belief that primary financial responsibility should rest with the individual, community, and state. We must have a variety of health services ready for the aged persons who need them.

We must have a nationwide educational program to demonstrate that preparation for later years must begin early—with emphasis physiologically in youth, economically during the earning period, and psychologically in middle years. We must continue to aid the voluntary health insurance industry as it develops new types of coverage for the aged.

These are just some of the positive steps that must be taken to meet the needs of older citizens in the long run, in a voluntary way and at the community and individual level. Granted it is not an easy, overnight task, and perhaps it does not have the "political appeal" of an expensive, federal medical care plan. However, I am convinced that such a program is in the best interests of all.

GUNNAR GUNDERSEN, M.D.
La Crosse, Wis.

ORGANIZATION SECTION

REGISTRATION AT THE CLINICAL MEETING, MINNEAPOLIS, DEC. 2-5, 1958

UNITED STATES

Alabama	5	Isthmian Canal Zone	0
Alaska	1	Kansas	11
Arizona	2	Kentucky	8
Arkansas	6	Louisiana	9
California	49	Maine	2
Colorado	11	Maryland	6
Connecticut	6	Massachusetts	16
Delaware	1	Michigan	43
District of Columbia	16	Minneapolis, Minn.	662
Florida	12	Minnesota	772
Georgia	3	Mississippi	5
Hawaii	1	Missouri	21
Idaho	6	Montana	19
Illinois	118	Nebraska	34
Indiana	30	Nevada	5
Iowa	108	New Hampshire	0
New Jersey	29	Washington	23
New Mexico	6	West Virginia	9
New York	77	Wisconsin	166
North Carolina	4	Wyoming	5
North Dakota	82	Total	2,628
Ohio	39		
Oklahoma	13		
Oregon	10	**OTHER COUNTRIES**	
Pennsylvania	50	Austria	1
Puerto Rico	3	Canada	21
Rhode Island	1	England	1
South Carolina	3	Ireland	3
South Dakota	62	Mexico	1
Tennessee	10	Nigeria	1
Texas	35	Switzerland	1
Utah	5	Thailand	1
Vermont	2	Total	30
Virginia	6		2,628
Virgin Islands	0	Grand Total	2,658

Numbers of Physicians and Guests Registered at Clinical Sessions

	Cleveland, Jan., 1948	St. Louis, Dec., 1948	Washington, D. C., 1949	Cleveland, 1950	Los Angeles, 1951	Denver, 1952	St. Louis, 1953	Miami, Fla., 1954	Boston, 1955	Seattle, 1956	Philadelphia, 1957	Minneapolis, 1958
Physicians												
First day	639	1,160	1,195	777	1,892	1,618	995	1,822	1,483	1,070	1,615	1,528
Second day	227	677	1,321	815	1,666	674	1,225	944	1,574	643	499	638
Two days	866	1,837	2,516	1,592	3,558	2,292	2,220	2,766	3,057	2,313	2,114	2,166
Third day	636	318	472	539	741	272	431	401	597	425	448	400
Three days	1,502	2,155	2,988	2,131	4,299	2,564	2,651	3,167	3,654	2,738	2,562	2,566
Fourth day	394	45	192	59	128	50	79	86	125	75	75	92
Four days	1,896	2,200	3,180	2,190	4,427	2,614	2,730	3,253	3,779	2,813	2,637	2,658
Guests												
First day	...*	...*	...*	736	1,499	1,007	1,199	1,852	1,732	1,164	1,537	1,206
Second day	...*	...*	...*	554	1,557	1,243	1,648	1,048	971	644	625	579
Two days	...*	...*	...*	1,290	3,056	2,910	2,847	2,900	2,703	1,808	2,162	1,785
Third day	...*	...*	...*	387	1,259	987	974	541	652	645	651	529
Three days	...*	...*	...*	1,677	4,315	3,897	3,821	3,441	3,355	2,453	2,813	2,314
Fourth day	...*	...*	...*	104	341	222	282	233	581	321	174	247
Four days	...*	...*	5,307	1,781	4,656	4,119	4,103	3,674	3,936	2,774	2,987	2,561
Technical exhibitors	...	...	...	...	...	...	674	574	730	450	936	590
Technical exhibitor's guests	...	...	...	...	...	...	209	206	192	245	340	216
Grand total	...	...	...	...	...	...	7,716	7,707	8,637	6,282	6,900	6,025

* No record.

CHANGE OF ADDRESS

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COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

The Seventh Annual Report of the National Intern Matching Program, submitted by Ward Darley, M.D., Executive Secretary, presents information of interest to the medical profession, medical educators, hospital administrators, and prospective interns. Because this report portrays the background, development, and current status of the NIMP, the Council on Medical Education and Hospitals has requested that it be published in THE JOURNAL *of the American Medical Association.*

EDWARD L. TURNER, *M.D., Secretary.*

SEVENTH ANNUAL REPORT OF THE NATIONAL INTERN MATCHING PROGRAM

Prior to the turn of this century American medical education took very little interest in patient contact and responsibility as a part of the preparation for the practice of medicine. This lack of interest was reflected in the development of the internship as a responsibility of the hospital, rather than of the medical school, and now, more than half a century later, even though participation in and responsibility for patient care are very much a part of the medical student's education and although nearly half of the internships in the United States are in medical school affiliated hospitals, the internship continues primarily as a hospital responsibility—but a responsibility with which medical schools, and medical students as well as hospitals, are concerned. It should be of interest to review the development of this three-way concern.

The American Medical Association gave official recognition to the internship in 1904. The first list of hospitals approved for internship training was published in 1914. It was not until 1920 that the number of available internships began to exceed the number of medical graduates available.[1] Since 1920, and with each succeeding year, this disparity has increased until now the annual number of internships available is nearly twice the number of U. S. medical graduates. As the result of this, the development of competition between hospitals and the resultant pressures on medical students to accept internships was inevitable. As these pressures grew, it was equally inevitable that the medical schools should take an increasing interest in assisting their graduates to obtain good internships.

The first definite effort to solve this problem was in 1945 when the Association of American Medical Colleges, the American Hospital Association, the American Protestant Hospital Association, the American Catholic Hospital Association, and the American Medical Association adopted what was known as the Cooperative Plan. This plan involved the voluntary participation of medical students, medical schools, and hospitals in a complicated set of arrangements that were supposed to operate without any centralized operating authority. While the result was an improvement over the pre-1945 situation, there still remained confusion with many instances of lack of understanding and cooperation. As the number of internships continued to move ahead of the number of available U. S. graduates, it became apparent that something more was needed.

This "something" was suggested in 1950 by Dr. F. J. Mullin [2] in the form of a nationwide plan in which the matching of student and hospital choices could take place free of pressures and premature commitments, together with a time schedule and a system of appointment and acceptance notification which would be reasonable and capable of central administration. This plan was tried in 1951 and was found to be sufficiently successful so that its basic principles have been adopted as standard practice. Great credit is due the hospitals and the medical students for their willingness to cast their lot with this enterprise.

The agency now responsible for the administration of the plan is known as the National Intern Matching Program (NIMP). The NIMP is an inde-

TABLE 1.—*General Results 1952-1958*

Yr.	Hospitals Participating	Intern Programs Offered	Total Positions Offered	Total Positions Filled	% Filled	No. of Unfilled Positions	Students Participating	Students Unmatched
1952	795	1,068	10,414	5,564	53	4,850	5,681	117
1953	808	1,102	10,971	5,744	52	5,227	6,033	289
1954	820	1,032	10,729	6,051	56	4,678	6,412	361
1955	814	1,056	11,075	6,379	58	4,696	6,713	334
1956	821	1,003	11,459	6,588	57	4,871	6,821	233
1957	822	1,052	11,804	6,539	55	5,265	6,923	384
1958	819	1,062	11,958	6,734	52	5,224	7,031	397

pendent corporation governed by a board of directors which has representation from the American Hospital Association, American Medical Association, American Protestant Hospital Association, Association of American Medical Colleges, Catholic Hospital Association, Student American Medical Association, and one medical student representing the medical student body at large. The Army, Navy, Air Force, Veterans Administration, and Public Health Service have liaison membership on the board.

The mechanism of the plan, although complicated in execution, is simple in theory. Basically NIMP acts as a clearing agency. Each participating student submits a confidential list to NIMP, ranking, in the order of his preference, the hospitals where he has applied for internship. He applies for any internship which interests him. Each participating hospital also submits a confidential list, ranking, in the order of its preferences, the students which have applied to it. The NIMP then matches the student with the internship he rates the highest, insofar as the hospital's relative evaluation of the student applicant makes this possible.

While previous reports of the NIMP [3] have given detailed descriptions of the mechanisms of matching, none are as easily understood as the one prepared by Dr. N. C. Webb Jr. at the time he was a student member of the NIMP board of directors and himself being matched to an internship.[4] The significant portion of Dr. Webb's description is reproduced herewith:

TABLE 2.—*Application per Student*

Yr.	No. of Students	No. of Applications	No. per Student
1952	5,681	21,728	3.8
1953	6,033	19,416	3.2
1954	6,412	21,579	3.4
1955	6,713	25,617	3.8
1956	6,821	29,474	4.3
1957	6,925	30,434	4.4
1958	7,031	32,690	4.6

TABLE 3.—*Percentage of Students Matched by Order of Choice*

Yr	First Choice	Second Choice	Third Choice	Fourth Choice or Lower
1952	84	10	3	3
1953	85	10	3	2
1954	82	11	4	3
1955	76	14	5	5
1956	74	15	6	5
1957	76	13	6	5
1958	74	14	6	6

TABLE 4.—*Hospitals Ranking of Students with Whom They Were Matched by Percentage*

Yr.	Matched from Rank Group I*	Matched from Rank Group II	Matched from Rank Group III	Other	Total
1956	61	24	11	4	100
1957	71	19	7	3	100
1958	67	22	8	3	100

*If hospital quota is 10, first 10 men on list form rank group I, numbers 11-20 rank group II, etc.

Student Confidential Preference Lists

Green	Smith	Jones
1. Mt. Sinai	1. Mt. Sinai	1. Internia
2. Internia	2. Internia	2. St. Joseph
		3. Mt. Sinai

Hospital Preference Lists

The number in parentheses shows the number of interns being sought by each hospital.

Mt. Sinai (2)	Internia (1)	St. Joseph (1)
1. Jones	1. Smith	1. Jones
2. Smith	2. Jones	
3. Green	3. Green	

Consider Green, whose first choice is Mt. Sinai, which offers two internships, and which has ranked him third. Unless either Jones or Smith get matched elsewhere, he cannot get in. He is also waiting at Internia, since it, offering but one internship, has shown preference for Smith and Jones, and, unless both Smith and Jones get matched elsewhere, Green is not in here yet either.

Consider Smith. He ranked Mt. Sinai first, and it ranked him second. Since Mt. Sinai offers two internships, Smith can be permanently "matched." Since Smith is now matched at his first choice hospital, his name is removed from Internia, his second choice, and Jones and Green slide up.

Now the situation looks like this (*indicates a permanent match):

Student Lists

Green	Smith	Jones
1. Mt. Sinai	*1. Mt. Sinai	1. Internia
2. Internia		2. St. Joseph
		3. Mt. Sinai

Hospital Lists

Mt. Sinai (2)	Internia (1)	St. Joseph (1)
1. Jones	2. Jones	1. Jones
*2. Smith	3. Green	
3. Green		

Consider Jones. Since the removal of Smith from Internia's list, Jones has moved up to top position. This is a permanent match, since it is Jones' first choice. Jones' name is removed from the Mt. Sinai list and from the St. Joseph list, since he is matched at a hospital he prefers to either of these.

Now the situation looks like this (**denotes filled hospital):

Student Lists

Green	Smith	Jones
1. Mt. Sinai	*1. Mt. Sinai	*1. Internia
2. Internia		

Hospital Lists

Mt. Sinai (2)	**Internia (1)	St. Joseph (1)
*2. Smith	*2. Jones	
3. Green	3. Green	

The removal of Jones' name from Mt. Sinai allows Green to slide up into second place. Since two internships are offered at Mt. Sinai, Green is a permanent match. Final results:

Mt. Sinai—Smith and Green
Internia—Jones
St. Joseph—none

The three students all were matched with their first choice hospital. In this example, we have seen how men "slide up" on hospital lists, as men above them are matched to hospitals more desired by those men. You will note that each

man holds his positions on the lists of the various hospitals until he becomes a permanent match. No one can "by-pass" a student on a hospital list. A student is removed from a hospital list only when he is matched with a hospital he prefers more. St. Joseph got no intern because its one applicant preferred Internia and was matched there.

This, the 1958 Matching Program's report, is the seventh consecutive year in which student and hospital choices have been matched without error. The success of each matching depends on the distribution of carefully prepared materials to medical students, medical schools, and hospitals, the meeting of deadlines on the part of students, hospital administrators, medical school deans, and the NIMP office, and the careful checking and rechecking of both student and hospital choices, both with the students and hospitals and within the mechanical system of the matching itself.

The steps essential to one complete program are as follows:

1. The hospitals and students make arrangements to participate in a given program during the winter and spring before the following cycle begins. The dates indicated are approximate as they vary slightly from year to year.

2. October: The hospital directory is published, containing a description of each participating hospital, the types of internships offered and the intern quota for each.

At the same time the student directory is published which contains the name and medical school of each participating student.

3. October 1–January 10: This is the period during which the students make application for internship to hospitals. The process of application, more often than not, involves personal visits to the hospitals in which the students are interested.

4. October 1–December 10: The deans send letters of recommendation to the hospitals so that insofar as possible the hospitals may have this information when the students are interviewed or are being considered for internship.

TABLE 5.—*Major Teaching Hospitals*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	39	897	897	100	45	1,224	1,224	100
99–50	58	1,962	1,457	74.3	78	2,528	1,976	78.2
49–01	40	930	289	31.1	22	526	182	34.6
0	12	87	0	0	6	47	0	0
Total	149	3,876	2,643	68.2	151	4,325	3,382	78.2

TABLE 6.—*Minor Teaching Hospitals*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	11	177	177	100	11	145	145	100
99–50	20	571	100	70.1	25	364	265	72.8
49–01	28	403	106	26.3	13	175	38	21.7
0	20	205	0	0	8	62	0	0
Total	79	1,056	473	44.8	57	746	448	60.1

TABLE 7.—*Nonaffiliated Hospitals*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	62	1,120	1,120	100	65	841	841	100
99–50	128	1,475	1,030	69.8	127	1,607	1,109	69.0
49–01	178	2,085	478	22.9	151	1,797	428	23.8
0	212	1,359	0	0	264	2,116	0	0
Total	580	6,039	2,628	43.5	607	6,361	2,378	37.4

5. January 31: Closing date for receipt at the NIMP office of student and hospital confidential rank order lists.

6. February 16: The confidential student list is confirmed to each student. Also, the confidential hospital list is confirmed to each hospital.

7. February 21: Closing date for accepting corrections to student or hospital confidential rank order lists.

8. February 23: The matching operation begins.

9. March 11: The results of the matching plan are mailed to medical school deans and to hospitals.

10. March 16: The results are given to the students by the deans. At the same time the hospitals receive their matching results.

11. March 16-26: The hospitals send contracts to matched students and students sign and return the contracts.

Except for tables 5 through 19, the tables and discussions that follow will continue the record about as it has been carried in previous reports.[5] The general statistics as shown in table 1 reveal no striking shifts over previous years. The number of unmatched students continues to be large because of the difficulty which foreign graduates have in competing with U. S. and Canadian students (152 out of all of the 397 unmatched students were graduates of foreign schools) for the more popular internships. In the program of 1959-1960 (the coming program), because screening by the Educational Council for Foreign Medical Graduates will be required for the registration of graduates from foreign schools, the number of foreign graduates participating in the program and *a priori*, the number going unmatched, will be sharply reduced. After 1959 the number of participating foreign graduates should begin to go up but also, because of the ECFMG screening, the percentage matched should be increased.

Table 2 reveals the trend for each student to apply to an increasing number of hospitals. Table 3 shows a slight continuation of the downward trend in students receiving their first choices. These two trends can be taken to indicate that students are adding, as first choice, institutions in which they may feel their chances of acceptance are open to question but also in which they would like to intern if they possibly can. A student can justify such "tries" because in doing so he knows that he is not hurting his chances for his second or third choice hospitals—hospitals which formerly he would have listed in first and second place.

Table 4 shows a slight drop in the percentage of hospitals receiving their highest choices of students. There is no logical explanation for this. The significant thing here is that the percentage of hospitals receiving the total of their first and second choices has remained essentially the same.

Tables 5 through 8 show hospitals classified according to medical school affiliation or nonaffiliation, the number of interns sought and obtained and the percentage of internships filled. The affiliated hospitals are broken down according to whether or not the degree of medical school control is of major or minor degree. The figures for the five-year period 1953 through 1958 show some very interesting trends:

Table 5, major affiliated hospitals: The total number of hospitals has remained essentially unchanged.

TABLE 8.—*Federal Services (Veteran's Administration Excluded)*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	5	497	497	100	4	526	526	100
99-50	1	40	20	50	...	...	...	...
49-01	10	198	53	26.8	...	...	...	...
0	3	50	0	0	...	...	...	...
Total	19	785	570	72.6	4	526	526	100

TABLE 9.—*Hospitals Offering Stipends up to Fifty Dollars*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	27	475	475	100	14	394	394	100
99-50	65	1,705	1,350	75.2	17	548	440	80.3
49-01	41	934	276	29.6	6	140	56	40
0	27	210	0	0	5	43	0	0
Total	160	3,414	2,101	61.5	42	1,125	890	79.1

TABLE 10.—*Hospitals Offering Stipends of from Fifty-one to One Hundred Dollars*

Quota Saturation Percentage	1953				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	40	736	736	100	26	637	637	100
99-50	59	940	647	68.8	42	1,178	867	73.6
49-01	107	1,357	289	21.3	26	417	100	24
0	118	802	0	0	59	577	0	0
Total	324	3,835	1,672	43.6	153	2,809	1,604	57.1

The total number of interns sought and the actual percentage matched has increased. The number of hospitals filling 50% or more of their quotas has increased and those filling 49% or less has decreased.

Table 6, minor affiliated hospitals: The total number of hospitals has decreased as has also the number of interns sought. The percentage of the total of interns matched over the number sought has shown an increase. The number of hospitals filling 50% or more of their quotas has remained essentially unchanged and those filling 49% or less has decreased.

Table 7, nonaffiliated hospitals: There have been no striking changes in any of these figures over the five year span.

Table 8, federal hospitals: Veterans Administration hospitals are not included here because students apply to the individual institutions rather than to this particular governmental service. As a consequence the Veterans Administration hospitals are distributed among the previous three groupings. The only notable change in the governmental services is that the percentage of interns matched over the number sought has gone from 72.6 to 100.

Tables 9 through 12 show hospitals classified according to monthly stipends offered, the number of interns sought and obtained, and the percentage of internships filled. Here again the figures for 1953 and 1958 show significant trends.

Table 9, hospitals offering less than $50 per month: The number of hospitals, for all levels of quota saturation, has dropped precipitously. The number of interns sought and matched has also dropped throughout. On the other hand, the percentage of total interns matched over the number sought has increased.

Table 10, hospitals offering between $51 to $100 per month: Here again the total number of hospitals for all levels of quota saturation has shown a sharp drop. Except for the quota saturation of from 99 to 50%, the number of interns sought at all levels has also dropped. But the total number of interns matched has remained essentially the same and the percentage of total interns matched over the number sought has increased.

Table 11, hospitals offering between $101 to $200 per month: The number of hospitals at each saturation level has increased significantly. At all saturation levels the percentage of interns matched over the number sought has remained essentially unchanged.

Table 12, hospitals offering more than $201 per month: The number of hospitals and the number of

TABLE 11.—*Hospitals Offering Stipends of from $101 to $200*

	1953				1958			
		Interns				Interns		
Quota Saturation Percentage	No. of Hospitals	Sought	Matched	% Matched	No. of Hospitals	Sought	Matched	% Matched
100	36	424	424	100	53	857	857	100
99-50	74	871	614	70.5	107	1,907	1,427	74.8
49-01	83	873	237	27.1	108	1,410	350	24.8
0	88	557	0	0	173	1,310	0	0
Total	281	2,725	1,275	46.8	441	5,484	2,634	48.0

TABLE 12.—*Hospitals Offering Stipends of $201 or More*

	1953				1958			
		Interns				Interns		
Quota Saturation Percentage	No. of Hospitals	Sought	Matched	% Matched	No. of Hospitals	Sought	Matched	% Matched
100	4	62	62	100	**26**	302	302	100
99-50	5	39	27	69.2	**62**	828	593	71.6
49-01	5	56	18	32.1	43	504	136	27
0	7	28	0	0	34	254	0	**0**
Total	21	185	107	57.8	165	1,888	1,031	54.6

TABLE 13.—*Number of Interns Sought, from One to Nine*

	1954				1958			
		Interns				Interns		
Quota Saturation Percentage	No. of Hospitals	Sought	Matched	% Matched	No. of Hospitals	Sought	Matched	% Matched
100	42	261	261	100	29	185	185	100
99-50	58	385	258	67	56	370	246	66.5
49-01	74	487	112	23	64	445	101	22.7
0	238	1,322	0	0	193	1,159	0	0
Total	412	2,455	631	25.7	342	2,159	532	24.6

interns sought and matched all show a very marked increase. Yet the percentage of internships filled over the number offered remains about the same.

Tables 13 through 16 show hospitals classified according to quota size, the number of interns sought and obtained, and the percentage of internships filled. It should be noted that the data cover a four-year instead of a five-year span (begins with 1954 instead of 1953).

Table 13, hospitals with from 1 to 9 interns: There has been a drop in the number of hospitals as well as in the number of interns sought at all quota saturation levels but at each level the percentage of the number of interns sought against the number matched has remained essentially the same.

Table 16, hospitals with 50 or more interns: The number of hospitals involved here continues to be small and none of the data for the four-year span show any significant change.

Thus, from the preceding three groups of data, it would appear (1) that the quota saturation percentage for the affiliated hospitals has been increasing and is more favorable than that for the unaffiliated; (2) that the federal services (Veterans' Administration excluded) are enjoying 100% quota saturation; (3) that, while more hospitals are offering higher stipends, the increasing high quota saturation for the low as compared to the high stipend hospitals shows that increasing numbers of graduates are attracted to an internship by factors other than stipend; and (4) that those hospitals with intern quotas of 20 or more are experiencing a much higher quota saturation than those with less.

Finally table 17 shows the distribution of the students matched as between those hospitals affiliated with their own school of graduation, hospitals not affiliated with their school of graduation but in the same state, hospitals not in the state of graduation, and the federal services (exclusive of the Vet-

TABLE 14.—*Number of Interns Sought, from Ten Through Nineteen*

Quota Saturation Percentage	1954				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	69	926	926	100	56	795	795	100
99-50	86	1,111	788	70.9	107	1,453	1,031	70.9
49-01	88	1,126	259	23	102	1,358	347	25.6
0	44	529	0	0	82	975	0	0
Total	287	3,692	1,973	53.4	347	4,581	2,173	47.4

TABLE 15.—*Number of Interns Sought, from Twenty Through Forty-Nine*

Quota Saturation Percentage	1954				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	29	838	838	100	33	1,009	1,009	100
99-50	43	1,287	1,004	78	55	1,648	1,292	78.4
49-01	30	880	275	31.3	17	528	142	26.9
0	2	40	0	0	3	91	0	0
Total	104	3,045	2,117	69.5	108	3,276	2,443	74.6

TABLE 16.—*Number of Interns Sought, Fifty or Over*

Quota Saturation Percentage	1954				1958			
	No. of Hospitals	Interns			No. of Hospitals	Interns		
		Sought	Matched	% Matched		Sought	Matched	% Matched
100	6	631	631	100	3	221	221	100
99-50	10	839	668	79.6	12	1,028	781	76
49-01	1	67	31	46.3	3	167	58	34.7
0	0	0	0	0	0	0	0	0
Total	17	1,537	1,330	86.5	18	1,416	1,060	74.9

centage of the number of interns sought against the number matched remains essentially the same.

Table 14, hospitals with from 10 to 19 interns: The number of hospitals receiving 100% of their quotas has dropped. For each of the levels below 100%, both the number of hospitals involved and the number of interns sought has increased and yet the percentage of the number of interns sought against the number matched has remained essentially the same.

Table 15, hospitals of from 20 to 49 interns: The number of hospitals receiving 50% or more of their interns has increased and those receiving 49% or less has decreased, but at all saturation levels the

erans Administration). The information really being sought here is the extent to which graduates tend to leave their own school's hospitals and communities for internship. Inspection of the table will reveal that, if the federal services are ignored, approximately half of the graduates intern outside of the state in which their school of graduation is located, one-fourth intern in the hospitals affiliated with their school of graduation, and the other fourth leave the hospitals of their school of graduation but still remain in the state.

TABLE 17.—*1958 Distribution Data—Numbers and Percentages Matched—All Schools of Medicine*

Total U. S. Graduates Matched from All Medical Schools	Hospitals Affiliated with School of Graduation		Hospitals Not Affiliated with School of Graduation but in Same State		Hospitals Out of State		Federal Service	
	No.	%	No.	%	No.	%	No.	%
6,347	1,545	24.3	1,399	22.0	2,885	45.4	518	8.16

TABLE 18.—*1958 Distribution Data—Numbers and Percentages Matched—Graduates of Privately Owned Schools of Medicine*

Total U. S. Graduates Matched from Privately Owned Medical Schools	Affiliated Hospitals of Own Medical School		Hospitals in Same State but Not Affiliated with own Medical School		Out of State Hospitals		Federal Service	
	No.	%	No.	%	No.	%	No.	%
3,451	925	26.8	651	18.9	1,641	47.6	234	6.8

Tables 18 and 19 show the breakdown of the above data as between graduates of publicly and privately owned schools. No striking difference between the two groups can be noted.

From the vantage point of seven years' perspective, it is indeed gratifying to witness the success of a complicated socioeconomic experiment of this type. It is one that justifies itself not only in the name of important service but also in the name of research data that are leading to a better understanding of a very important aspect of medical education and service.

TABLE 19.—*1958 Distribution Data—Numbers and Percentages Matched—Graduates of Publicly Owned Schools of Medicine*

Total U. S. Graduates Matched from Publicly Owned Medical Schools	Affiliated Hospitals of Own Medical School		Hospitals in Same State but Not Affiliated with Own Medical School		Out of State Hospitals		Federal Service	
	No.	%	No.	%	No.	%	No.	%
2,896	620	21.4	748	25.8	1,244	43.0	284	9.8

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COUNCIL ON INDUSTRIAL HEALTH

TONOMETRY IN GLAUCOMA SURVEYS

This report has been prepared by the Committee on Industrial Ophthalmology of the Council on Industrial Health, American Medical Association.

B. DIXON HOLLAND, M.D., *Secretary.*

The primary objective of any glaucoma survey is to discover all cases of undiagnosed glaucoma possible but not to treat, observe, or study the course of known glaucoma cases. Such a survey is most effective when the greatest number of individuals are adequately examined in the shortest possible time and with the least disturbance to their routine, by a minimum of personnel and with the minimum of equipment. The Committee feels that tonometry, the measurement of intraocular tension, is a safe procedure when properly performed by a person trained in the method and the program set up under the guidance of a consulting ophthalmologist and is the best of the various screening methods to employ in a glaucoma survey.

The members of the Committee on Industrial Ophthalmology are Edmund B. Spaeth, Chairman, Philadelphia; Franklin M. Foote, New York; Ralph S. McLaughlin, Laconia, N. H.; Joseph F. Novak, Pittsburgh; Ralph W. Ryan, Morgantown, W. Va.

BUREAU OF MEDICAL ECONOMIC RESEARCH

CRITIQUE OF SOME STATISTICS ON HEALTH INSURANCE AMONG THE AGED

Walter Polner, Ph.D., Chicago

National surveys of households now show a growing number of persons 65 years of age and over who own voluntary health insurance. By themselves, these figures on the total aged population understate the true extent of this coverage, since sizable groups among the aged do not wish to purchase this type of voluntary insurance. An analysis of these groups who have other alternatives will clarify the meaning of existing statistics on the extent of voluntary health insurance coverage of the entire aged population.

All are aware that the aged have heterogeneous attitudes toward working, housing, religion, leisure, and eating. There is little reason to believe that they maintain a homogeneous attitude toward the purchase of voluntary health insurance. Since some individuals during working life do not wish to purchase any insurance even though physically eligible and financially able, it is not surprising that there are also groups among the elderly who hold similar ideas on the purchase of voluntary health insurance. Yet there are certainly some aged who desire this insurance but are unable to obtain it; there are also some who consider that they have other means of paying for care.

The population 65 years of age and over increased to 15 million in 1958. There is every indication that this rapid change in number has brought a new interest in the study of behavior patterns of the aged. Specialists in many fields—sociologists, psychologists, political scientists, psychiatrists, economists—have presented studies on particular aspects of this increasingly important section of the population. For such specialists, however, there is a danger of considering all aged persons as identical units instead of as individuals.

The aged have two major elements in common—the number of years they have lived, which makes them alike, and the fact that they are human beings, which means they vary as widely in income, living conditions, needs, desires, and social attitudes as any other group in the population. Their earning power in the years preceding retirement varied sharply. Those who retired during the depression of the 1930's had fewer opportunities to save for old age than the wage earners now approaching retirement. The latter probably accumulated during the recent period of great postwar prosperity far more assets, such as life insurance, traditionally important in meeting the expenses of the last illness.

Consideration of the aged population as a whole, a group distinct in certain ways from the population under the age of 65, can be a valid method of studying a problem. But with a group involving so many individuals we must beware of concentrating all of our attention on this approach alone. It is only one of several ways of dealing with a question.

This warning note can well be sounded in reference to the amount of voluntary health insurance for persons 65 years of age or over. Numerous studies on the extent of voluntary health insurance for the aged have resulted in various estimates of the number of persons covered. A report from the insurance department of New York State, based on extensive studies by experts, states, ". . . somewhere in the order of 35 per cent of the New York State population 65 years of age and over have hospital expense insurance."[1] Such a statement from the insurance department of our most populous state carries weight, and it has been quoted extensively.[2] Even if we accept this estimate as accurate, its usefulness is doubtful unless it is taken in full context.

Voluntary health insurance is not a phenomenon related only to the age of the person covered. An understanding of voluntary health insurance coverage of the aged should include not only the numbers actually covered, but also the possible market for such coverage. How many of the aged want this insurance? How many feel no need for it, either because they can finance their own medical and hospital care or because cost of such care is met from other sources? How many are actually opposed to such insurance? Thirty-five per cent of what? These

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are questions which must be explored before any estimate of the extent of present coverage can be meaningful.

Groups Among the Aged

Who are the aged who are not interested in the purchase of voluntary health insurance? Their exact number cannot be stated, since some with alternative means of obtaining care may still purchase insurance. Some aged veterans, for instance, may be satisfied with the potential protection afforded by Veterans Administration hospitals. Other veterans may purchase insurance so that they may be assured of private treatment.

Classification of the aged into groups that are potentially outside the market for voluntary health insurance coverage can be made. Roughly five main categories seem to be involved: (1) those who receive care from local or national programs for the indigent; (2) those who receive care through some other program supported entirely by the federal government; (3) those who receive care under private nonvoluntary health insurance mechanisms; (4) those in institutions; and (5) those who oppose voluntary health insurance as a solution to their problems.

Public Aid Programs for Indigent Aged.—Persons receiving old-age assistance probably comprise the largest group outside the market for voluntary health insurance. In June, 1958, it included almost 2,500,000 individuals, few of whom have such coverage. Since there is a wide variety of medical care programs for public assistance recipients, only a few (probably less than 10%) of those indigent aged would consider it necessary to lower their standard of living by spending a portion of the assistance grant on insurance. In addition, other programs cover the aged receiving aid to the blind, aid to the totally and permanently disabled, and the indigent aged not qualified for any of the mentioned programs but aided by state and locally financed general assistance programs. For each of these groups, medical and hospital care (varying in comprehensiveness from state to state) is available at government expense.

Other Federally Supported Programs.—Groups eligible for care at federal expense are the aged veterans who consider the Veterans Administration hospital system as their "insurance" against medical expense; some dependents of servicemen who receive care through Medicare; retired military personnel as well as their dependents, especially those living near military medical facilities who can receive treatment therein; those Indians who can receive treatment under the auspices of the Division of Indian Health of the Public Health Service; merchant seamen and others eligible for care through the hospitals of the Public Health Service.

Other Programs.—There are retirees who can receive medical services as part of their retirement plans by means of insurance mechanisms other than voluntary health insurance to pay for medical and hospital service. Some firms provide employees with group life insurance which provides that the face amount may be reduced to pay hospital and medical bills. These persons have the means of payment but not "voluntary health insurance" provided for them.

Institutional Population.—The aged persons in mental and tuberculosis hospitals and sanitariums, county and state homes, government or private homes for the aged, and state or federal prisons are not now in the market for voluntary health insurance.

Opposition to Voluntary Health Insurance.—Some of the aged have religious reasons for opposition to the purchase of voluntary health insurance. They will be found among those members of religious orders which provide hospital and medical services; those with religious beliefs who do not see any necessity for voluntary health insurance; and those belonging to sects which do not consider the normal services of the physician and hospital necessary, such as various groups on the West Coast and in the Appalachian Mountain region.

Some aged are opposed to insurance per se as a means of financing any contingency, including health problems. The size of this group among the aged cannot be estimated, but it exists in the general population and, therefore, certainly carries over into the aged group.

In addition there are aged who carry insurance but not voluntary health insurance—preferring other means of meeting health costs. For such groups the idea of postpayment of medical and hospital bills may have more appeal than a prepayment system. As the working period of life recedes, the appeal of prepayment over postpayment may diminish. The use of other assets, such as savings or life insurance, may be more meaningful to them than the present voluntary health insurance system.[3]

The existence of this last group is substantiated by a recent study of the aged population of Bloomington–Normal, Ill. This study, which divided the aged population into four socioeconomic groups, indicated that proportionately less voluntary health insurance was held by the "well-to-do" group than

by those in the "comfortable" income group. The author of the study states, "The few persons in Group IV [well-to-do] having insurance is probably due to the lack of concern on their part regarding medical expenses." [4] This may be an oversimplification. This "well-to-do" group may also have less inclination to use the health insurance mechanism because of their social attitude toward health insurance, their health status, their relations with physicians, and their family situation.

The question of income of the aged population is important, but dependable data on the subject are lacking. Recent studies have shown that there is a portion of the aged population having a residue of income, assets, and resources. Using income tax data as a basis for his study, Prof. James Brunner states, "These data are in apparent conflict with the general assumption that the aged either receive no income or that the amount is very low . . . what is also overlooked is the presence of these older persons in the higher income groups." [5] These well-to-do older people may feel less need for the insurance mechanism in meeting health needs.

Comment

These categories can probably be expanded; on the other hand, there is probably a certain amount of overlapping among the various groups listed. Exact statistics on the number of persons eligible for care through governmental or private programs or those opposed to the use of voluntary health insurance are impossible to obtain. If we consider that the largest group countable (the old-age assistance recipients) comprises almost 2,500,000 people, the maximum number of the 15 million aged persons who are now in the market for voluntary health insurance would be approximately 12,500,000. When the other aged persons in the groups listed are added to the old-age assistance group the 12,500,000 estimate will undoubtedly be very much lower. How much lower will depend on an accurate count of these aged persons. In terms of the group that believes in and is potentially in the market for health insurance coverage, elimination of these aged persons may remove a significant number from the voluntary health insurance market at the present time.

Already studies show 45% of the larger population over 60 have some type of voluntary health insurance.[6] There is a growing tendency for the group approaching retirement to hold on as much as is possible to such insurance. As more people have an opportunity to obtain this coverage in their working years and develop a belief in its usefulness, there is hope that the next decade will see most of those who desire voluntary health insurance able to obtain it at reasonable rates and without a major change in the present insurance pattern. There is also hope that those who depend on voluntary means other than health insurance also will be increasingly able to meet their medical and hospital bills during retirement without recourse to government programs. In this complex problem of the aged, "we must be wary" as Alfred North Whitehead warned, "of the error of thinking that the facts are simple because simplicity is the goal of our quest." [7] Research in this field is still difficult, and factual data are incomplete. We must continue, in his words, "to seek simplicity and distrust it."

Summary

When dealing with a large population group it is necessary to determine clearly the homogeneity of the group. The simple method of lumping together heterogeneous elements for the sake of ease of expression does not lead to understanding. It would be erroneous to believe that all the aged desire to provide for their hospital and medical bills by voluntary health insurance. Therefore, the figures on voluntary health insurance for the total aged population based on household surveys do not tell the entire story of the progress in coverage that has been accomplished in the 1950's. The resulting percentages, such as 35, are far too low, as the unmet problem is far less than 65%.

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MEDICAL NEWS

ARKANSAS

Dr. Day Goes to Washington.—The University of Arkansas Medical Center, Little Rock, held a convocation recently honoring Paul L. Day, Ph.D., member of the faculty for 31 years who has resigned to become scientific director of the U. S. Food and Drug Administration, Washington, D. C. Dr. Day has been chairman of the school's department of biochemistry since coming to Arkansas in 1927. Dr. F. Douglas Lawrason, provost for medical affairs, presided at the convocation. A faculty dinner honoring Dr. Day was held Dec. 29.

CALIFORNIA

Physicians Meeting in Palm Springs.—The American College of Physicians, Southern California Region, will meet at the El Mirador Hotel, Palm Springs, Feb. 7-8. The program has 30 papers on the scientific program, including the following:

Pre- and Post-Natal Development of the Human Lung, Dr. Clayton G. Loosli, Los Angeles.

Thyrotoxic Myopathy, Dr. Howard P. Lewis, Portland Ore.

Concepts and Misconceptions about Coccidioidomycosis and Coccidioides Immites, Dr. Roger O. Egeberg, Los Angeles.

A banquet, Feb. 7, 7:30, will have Dr. George C. Griffith, governor of the college for Southern California, as toastmaster and Horace W. Magoun, Ph.D., professor of anatomy, University of California School of Medicine, Los Angeles, speaking on "The Rise of Russian Science and Physiology." Special guests will include Drs. Dwight L. Wilbur, president, American College of Physicians, and Howard P. Lewis, president-elect of the college.

Psychiatry in General Practice.—The second Postgraduate Seminar on Psychiatry in General Practice of the Southern California Psychiatric Society, Southern California District Branch of the American Psychiatric Association, in conjunction with the General Practice Section of the Los Angeles County Medical Association will be held Jan. 31-Feb. 1 at the Los Angeles County Medical Association auditorium, 1925 Wilshire Boulevard, Los Angeles. The two-day session which will be devoted to discussions of psychiatric problems in the everyday practice of the general practitioner of medicine. Representatives of psychiatry and medicine in the Los Angeles area will speak and lead the discussions. Registration will be open to all qualified physicians and credit will be given for attendance in category II of the American Academy of General Practice. For information, write to Southern California Psychiatric Society, 427 N. Camden Drive, Beverly Hills, Calif.

Directory of Heart Clinics.—Twenty-four cardiac clinics serving heart patients in Los Angeles County have been certified by the Los Angeles County Heart Association as meeting standards to provide the best care for heart patients. The disclosure was made recently with the publication of a Cardiac Clinic Directory by the association as a community service. The heart association said 10,000 copies are being distributed without charge to physicians, nurses, and health and welfare agencies in this area. Certification of clinics, a year-around activity of the association's Cardiac Clinics Committee, is a community service "to guarantee the best possible patient care." The directory was financed by the Wyeth Laboratories of Philadelphia. Dr. George C. Griffith, association president, said the directory reflects a nine-year effort by the association to encourage the improvement of existing facilities and the establishment of more cardiac clinics. Developed and edited by the Cardiac Clinics Committee, of which Dr. Sim P. Dimitroff is chairman, the directory serves as a guide for professional referral to clinics for children and adults. It also lists specialized services in cardiology, rheumatic fever, prophylaxis, evaluation for surgery, and cardiopulmonary function studies.

Begin Construction on Two Medical Center Buildings.—Construction of the second and third buildings of the University of Southern California Medical Center has begun. The more than 3-million-dollar project includes a six-story medical research building, a two-story instructional building, and the control center wing connecting the two. The research structure will be known as the Seeley Wintersmith Mudd Memorial Laboratory of the Medical Sciences in honor of the late Colonel Mudd, mining engineer and leading citizen of Los Angeles. It is being built with funds provided by his son, Dr. Seeley Greenleaf Mudd, vice-chairman of the board of trustees of the university and former dean of the School of Medicine, and by the U. S. Public Health Service. The basic sciences teaching building is being built with funds contributed by graduates of the School of Medicine, students, faculty members, and friends. When the buildings

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

are completed in February, 1960, it will be possible for the first time for the School of Medicine to consolidate a majority of its teaching and research in one location. At present, the two years of medical instruction in the basic sciences are given on the main university park campus. The Seeley Wintersmith Mudd Memorial Laboratory Building will contain 49 laboratories, offices, and specialized chemical and physiological research facilities. The top floor has been reserved for the exclusive use of visiting scientists from this country and abroad who will be invited to lecture and to continue research work in their chosen fields at the School of Medicine. The instructional building will have 10 laboratories, two lecture rooms, anatomical laboratories, and other teaching quarters. The two buildings comprise more than 87,000 square feet of floor space, and will be completely air-conditioned.

COLORADO

Clinical Meeting in Denver.—The 24th midwinter clinical session of the Colorado State Medical Society will be held in Denver Feb. 17-20 at the Shirley Savoy Hotel. The program will feature panel discussions on "Perinatal Morbidity and Mortality" Feb. 18, with Drs. Ralph C. Benson, of Portland, Ore., and Woodruff L. Crawford, of Rockford, Ill., as guest speakers for that section. On Feb. 19, the panel will concern itself with "The Acute Abdomen," featuring Drs. Webster H. Brown, of Baltimore, and Philip Thorek, of Chicago, as guests. Feb. 20, the panel is divided into two sections, the first on wrist and ankle fractures, and orthopedic and rehabilitative problems associated with such injuries, and the second primarily concerned with the medicolegal aspects of neck injuries. Drs. William H. Bickel, of Rochester, Minn., and Miland E. Knapp, of Minneapolis, will be featured on both portions of the panel. February 17 will be devoted to an all-day orientation course for new members of the society and the opening session of the House of Delegates. Social activities are planned. Physicians in Denver during the meeting are cordially invited. A registration fee of $5 is charged all physicians.

ILLINOIS

Hospital Lecture.—The fifth lecture in the ninth annual North Shore Hospital lecture series on "Emotional Forces in the Family" will be held at the hospital, 225 Sheridan Road in Winnetka, Feb. 4, 8:00 p. m. "The Impact of Relatives and In-Laws" will be discussed by Dr. Nathan W. Ackerman, New York City, associate clinical professor of psychiatry, Columbia University, and president, Association for Psychoanalytic Medicine. The Commission on Education of the American Academy of General Practice has approved these lectures for category II credit. Dr. Ackerman has agreed to answer questions after his presentation. Physicians and allied professional personnel are invited.

KENTUCKY

Dr. Kuhns Honored.—Dr. Dwight M. Kuhns, director of laboratories, Harlan Memorial Hospital, Harlan, was presented the Carlos J. Finlay gold medal and certificate of the National Order of Merit "Carlos J. Finlay," at the Academy of Science, Havana, Cuba, Dec. 3. This award was given "for contributions to the control of meningococcal meningitis and bacillary dysentery." Carlos J. Finlay was the original author of the later proved mosquito transmission theory of yellow fever. Dr. Kuhns is a retired colonel of the U. S. Army Medical Corps.

MARYLAND

Dr. Sulzberger to Give Ketron Lecture.—The third Lloyd W. Ketron Lecture will be given by Dr. Marion B. Sulzberger Feb. 19 at Hurd Hall, Johns Hopkins Hospital, Baltimore, on "Some New Findings Concerning the Biology of the Skin Surface."

MICHIGAN

Dr. Davies Gives South American Lectures.—Dr. Windsor S. Davies, clinical professor of ophthalmology, Wayne University College of Medicine, Detroit, invited by the Pan-American Ophthalmological Society to give lectures in six South American countries, left Detroit Dec. 27 for the month-tour. He lectured before ophthalmological groups in Rio de Janeiro and Sao Paulo, Brazil; Montevideo, Uruguay; Buenos Aires, Argentina; Santiago, Chile; Lima, Peru; and Bogota, Colombia, on "Diseases of the Macula and Anterior Chamber Epithelium."

Open Center for Alcoholism.—A formal recognition program honoring the opening of a new treatment center for alcoholism was held at Wayne University College of Medicine, Detroit, Jan. 12. The Alcoholic Center, which opened Jan. 13, will be part of Receiving Hospital's outpatient clinic directed by the department of psychiatry of the university. Dr. Melvin L. Selzer, of the department of psychiatry, University of Michigan, Ann Arbor, gave a talk on "Problems of Aggression in Psychotherapy with Alcoholics." Financial backing has been given by the Michigan State Board of Alcoholism. Dr. James H. Graves, clinical director of the hospital's department of psychiatry and assistant professor at the university, will administer the program, which will give long-term and specialized care for a selected group of alcoholics. Wayne medical students participating will then evaluate different types of psychiatric treatment utilized.

MISSISSIPPI

Dr. Holland Comes to Mississippi.—Dr. William C. Holland, a member of the pharmacology department faculty at Vanderbilt University School of Medicine since 1950, has been named professor of pharmacology and chairman of the department at the University of Mississippi School of Medicine, Jackson. He replaces James C. Rice, Ph.D., who retired Dec. 31.

NEW YORK

Foreign Lecturer.—James F. Danielli, Sc.D., physiologist specializing in cytochemistry and professor of zoology, King's College, London, England, will speak at the State University Upstate Medical Center, Syracuse, March 16, 17, and 18 and will deliver a lecture the evening of March 17, 8:30 p. m., on "Designing of Drugs for the Chemotherapy of Cancer." Dr. Danielli is one of 16 scientists who will deliver Squibb Centennial Lectures in 76 medical schools this winter. E. R. Squibb and Sons has arranged the lectures to commemorate the firm's 100th anniversary.

Cardiac Teaching Day.—The third annual Cardiac Teaching Day sponsored by the Broome County Medical Society will be held Feb. 4 in the Arlington Hotel, Binghamton. Dr. Dwight E. Harken, associate clinical professor of surgery, Harvard Medical School, Boston, will present "The Pathology of Acquired Valvular Disease" and "Heart Surgery," both of which are motion-picture demonstrations. Dr. Laurence B. Ellis, associate clinical professor of medicine, Harvard Medical School, will present "Hemodynamic and Clinical Evaluation of Patients with Heart Disease" and "Late Improvement and Deterioration of Patients Who Have Had Heart Surgery." The third speaker on the program, Dr. Leroy D. Vandam, clinical professor of anesthesia, Harvard Medical School, will present "Safe Conduct of the Poor Risk Patient Through Surgery" and "Cardiac Arrest and Resuscitation." The program will conclude with audience participation and questions. For information write Mr. Charles Bishara, Executive Secretary, Broome County Medical Society, 42 Front St., Binghamton, N. Y.

New York City

Dr. Goodman Lectures in Africa.—Dr. Herman Goodman, of New York City, is visiting north and northwest Africa, the Belgian Congo, and the Indian Ocean cities of the continent January and February. He accepted invitations to informal discussions with health officials and physicians in Casablanca, Dakar, Accra, and Brazzaville. He will lecture before the local branches of the British Medical Association at Nairobi and Mombasa. Dr. and Mrs. Goodman had visited south and southeast Africa early in 1958 at the close of a round-the-world trip via Fiji, New Zealand, and Australia.

Dr. Weeden Cited.—Dr. Willis M. Weeden, medical director, Workmen's Compensation Board, New York State Department of Labor, was given a special citation "for meritorious service in appreciation of his exceptional contributions in advancing the employment of the physically handicapped." The citation, awarded by President Eisenhower's Committee on Employment of the Physically Handicapped, was presented to Dr. Weeden by Dr. Gerald D. Dorman, of New York City, chairman, New York State Medical Society's Council Committee on Workmen's Compensation, during a luncheon held as part of a two-day Institute on Workmen's Compensation.

Tuberculosis in New York City.—The number of tuberculosis deaths in New York City increased slightly in 1957, the first increase in more than a decade, according to the 1957 TB yearbook, published recently by the New York Tuberculosis and Health Association, which contains the 39th annual statistical review of this disease published by the organization. The 982 tuberculosis deaths recorded in 1957 compare with 974 in 1956. Manhattan's mortality was more marked than for the city as a whole. Whereas 365 Manhattan residents died because of tuberculosis in 1956, the number in 1957 rose to 421, an increase of 15%. During the 1957 calendar year 6,117 new tuberculosis cases were reported, compared to 6,137 the previous year. However, 16 of the city's 30 health center districts had more new cases reported in 1957 than in 1956. It was pointed out that there are certain sections of the city where the tuberculosis rate is as high, or even higher, than it was 30 years ago. Of those cases listed in the central tuberculosis register of the Department of Health on the last day of the year, 49% were residents of the Borough of Manhattan, 25% of Brooklyn, 13% of the Bronx, 12% of Queens, and 1% of Richmond.

NORTH CAROLINA

Conference on Occupational Health.—The University of North Carolina School of Medicine, Chapel Hill, will be host to the third annual Governor's Conference on Occupational Health, Feb. 5. This conference is sponsored by the North Carolina Occupational Health Council and will present a program featuring leaders in industry and industrial health in North Carolina and the nation.

Personal.—Dr. Keith S. Grimson, professor of surgery, Duke University Medical Center, Durham, has become chairman of the American Heart Association's Council for High Blood Pressure Re-

search, succeeding Dr. Eric Ogden, of Ohio State University. Dr. Grimson served last year as vice-chairman.—Dr. Howard H. Bradshaw, director, department of surgery, Bowman Gray School of Medicine, Winston-Salem, has been named chairman of the board of governors of the American College of Surgeons. He had been secretary since 1954 and is a founding member of the North Carolina Sectional Chapter of the congress.

PENNSYLVANIA

Dr. McCall to Come to Pittsburgh.—Dr. Milton L. McCall, currently on the staff of Louisiana State University School of Medicine, New Orleans, has been appointed medical director of Elizabeth Steel Magee Hospital and chairman, department of obstetrics and gynecology, University of Pittsburgh School of Medicine. The joint appointment becomes effective July 1. Dr. McCall, who previously served on the faculty of Jefferson Medical School and on the staff of Philadelphia General Hospital, for the last five years has been head of the department of obstetrics-gynecology at Louisiana State University. He has also served as obstetrician and gynecologist in chief of the university unit of Charity Hospital in New Orleans.

Philadelphia

Campaign for I. S. Ravdin Institute.—The campaign to raise $7,300,000 for the University of Pennsylvania's I. S. Ravdin Institute and a new residence for student nurses of the Hospital of the University of Pennsylvania is being accelerated in its final seven months with more than $5,750,000 already contributed. With 78% of the goal accomplished, and anticipating raising the remainder by July 1, 1959, ceremonies were held Dec. 19 marking the beginning of demolition of the old nurses' residence to make way for the Ravdin Institute construction. Division of the funds to construct the two new buildings provides for $5,730,000 for the institute and $1,570,000 for the Hospital School of Nursing student nurses' residence. Ground was broken for the residence at the Kings Court site Nov. 25. Named for the University of Pennsylvania surgeon, Dr. I. S. Ravdin, the 224-bed institute will increase the patient capacity of the Hospital of the University of Pennsylvania to about 950. The Ravdin Institute will include laboratories for medical students and residents and special teaching facilities.

Dedicate Mental Health Center.—Pennsylvania Hospital has formally dedicated its new Mental Health Center at 49th Street and Haverford Avenue and adjoining the Institute of Pennsylvania Hospital. Ceremonies featuring Mayor Richardson Dilworth as the principal speaker climaxed plans started in 1957. The center, completed at a cost of about $3,365,000, will consolidate the hospital's West Philadelphia department formerly operated in two separate units. The new building, air-conditioned throughout, is comprised of two sections. One, a five-story wing, has accommodations for 120 patients, each room with a private bath. Dining and lounging areas are located on every floor. In another two-story section is located an "activities center," which includes a lobby, an occupational therapy department, an auditorium and gymnasium, a music room, and other facilities. Doctors' offices are also in this area. Funds were derived from several sources. Sale of the 44th Street property realized $1,173,000. A federal grant under the terms of the Hill-Burton Act supplied about one million dollars; a grant from the Ford Foundation amounted to $152,000. About $300,000 was available from other sources.

TEXAS

Symposium on DBI in Houston.—Baylor University College of Medicine with the Houston Society of Internal Medicine and the Houston Area Diabetes Association will sponsor a symposium on a new oral hypoglycemic agent, Phenformin (DBI), to be held at the Houston Academy, Feb. 5-6. The program, directed by Dr. Max Miller, Cleveland, will comprise four panel discussions on the chemistry, pharmacology, toxicology, clinicometabolic investigation and clinical evaluation of DBI in the management of diabetes mellitus, including consideration of the special problems in diabetes. More than 50 investigators in diabetes will participate in the symposium.

UTAH

Memorial Foundation.—The University of Utah College of Medicine, Salt Lake City, has announced that medical research in Utah in industrial medicine will receive impetus through the newly-organized Richards Memorial Medical Foundation, which came officially into being shortly before the death of Dr. Paul S. Richards, Sr., one of the sponsors, along with his brother, Willard B. Richards, Jr., president of the Granite Furniture Co. One of the first goals of the foundation is establishment of a professorship of occupational disease in the University of Utah College of Medicine.

WISCONSIN

Rehabilitation Center for Milwaukee.—Construction of a complete rehabilitation center within the Milwaukee County General Hospital has been announced by John W. Rankin, director of the Milwaukee County Institutions and Departments. The facility will include all physical restoration, vocational evaluation, psychological and social services, as well as an associated sheltered workshop. Applications for key positions in the rehabilitation cen-

ter are being accepted as it is anticipated the center will open in the summer of this year. The center was made possible by grants from the federal and state vocational rehabilitation departments. Through the Milwaukee County institutions and departments it will be affiliated with the Marquette University School of Medicine, which plans to use it as a teaching and training center for medical students, physicians, and specialists. Dr. Robert W. Boyle, director of physical medicine, will be in charge of the facility.

GENERAL

Funds Available for Blood Research.—The Leukemia Guild of Missouri and Illinois has announced that they will have about $100,000 available for grants on July 1, to be allocated for investigative work in blood dyscrasias. Application forms are available upon request for filing on or before March 15. Applicants should include a description of research problem to be undertaken, institution in which research is to be carried out, personnel and equipment required to meet the needs of the problem, and amount of time and money needed for fruition. Requests for grants under $15,000 per year will be given preference. Address communications to: Mr. Ralph Shower, Executive Director, Leukemia Guild of Missouri and Illinois, 4530 Forest Park Blvd., St. Louis 8.

A. M. A. Grants-in-Aid for Research.—The Committee on Research of the American Medical Association has announced that the Subcommittee on Grants-in-Aid is prepared to make grants up to $500 in 1959 to supplement clinical and basic medical science research. Grants will be made for the purchase of supplies, animals, and equipment but are not intended for the payment of salaries of full- or part-time secretarial or technical help, labor or overhead. No more than two awards will be made to any one institution. The tentative closing date for the receipt of applications has been set for April 1. More complete information concerning the program and application blanks may be obtained by writing the Secretary, Committee on Research, American Medical Association, 535 N. Dearborn St., Chicago 10.

Radiology Meeting in Chicago.—The regular annual meeting of the members and fellows of the American College of Radiology will be held Feb. 6-7 at the Drake Hotel, Chicago. The afternoon of Feb. 6 a panel discussion will be conducted on the college "Principles of Ethical Radiological Practice," under the direction of Dr. Vincent W. Archer, college president. A luncheon will be given at the Drake Hotel that afternoon and the convocation that evening. The annual Teachers' Conference will be conducted Feb. 7 organized by the Committee on Education, with Dr. Philip J. Hodes as chairman. The topic will be "Radiobiology in Medicine," and 15 individual round-tables, with 10 participants per table, will be held. For information write Mr. William C. Stronach, Executive Director, The American College of Radiology, 20 N. Wacker Drive, Chicago 6.

Psychiatric Research Meeting in New York City.—The 17th scientific meeting of the Eastern Psychiatric Research Association, Inc., will be held Feb. 6, 8 p. m., at the New York University Medical School Alumni Hall A. The program will open with a film, "Migraine Equivalents." Papers will include "Empathic Communication and Anxiety in Medical Students," by Morris Weinstein, Ed. D., assistant professor of psychology, department of psychiatry, Albany Medical College, and "The Phenomenon of Chelation and Its Relation to Mental Disorders," by Dr. John C. Saunders, research scientist (pharmacology), Rockland State Hospital, Orangeburg, N. Y. Dr. Robert H. McCarter, Boston, will discuss Dr. Weinstein's paper, and Dr. George A. Jervis and Fred B. Goldstein, Ph.D., Thiells, N. Y., will discuss Dr. Saunders' paper. A business meeting will conclude the program. For information write Dr. David J. Impastato, 40 Fifth Ave., New York City, Secretary.

University Surgeons Meeting in Denver.—The 20th annual meeting of the Society of University Surgeons will be held Feb. 12-14 at the University of Colorado Medical Center, Denver, under the presidency of Dr. C. Rollins Hanlon. The program will open with addresses by Mr. Quigg Newton, president, University of Colorado; Dr. Robert Glaser, dean, University of Colorado School of Medicine; and Mr. Robert Denholm, administrator, University of Colorado Medical Center. A symposium on the "Problem of the Disappearing Service Patient in a University Surgical Training Program" the afternoon of Feb. 12 will be conducted under the chairmanship of Dr. Henry Swan, of Denver. Papers to be introduced by members include "Pituitary–Adrenal Response Following Trauma to the Isolated Leg," by Dr. R. H. Egdahl, Richmond, Va., and "Tumor-Host Relationship Factors in Man," by Drs. J. T. Grace, Jr. and A. Lehoczky, Buffalo, N. Y. The annual business meeting will be held the afternoon of Feb. 13 with the annual dinner held that evening. For information write Dr. Marshall J. Orloff, University of Colorado Medical Center, 4200 E. Ninth Ave., Denver 20, Colo.

Bahamas Medical Conference.—The seventh Bahamas Medical Conference will be held March 30-April 12 at the British Colonial Hotel, Nassau, Bahamas. The program will include the following topics and speakers:

(1) Pitfalls in the Evaluation of New Drugs; (2) New Developments in Cancer Chemotherapy, Dr. Thomas C. Fleming, Evansville, Ind.
Host Reaction in Infectious Diseases, Dr. William F. Kremer, Hartsdale, N. Y.
Epidemiology of Essential Hypertension, Dr. Marvin Moser, Valhalla, N. Y.
(1) Degenerative Vascular Changes in Diabetes; (2) Some Problems Associated with Adreno-Cortical Activity, Dr. Harold Rifkin, New York City.
(1) Congenital Aortic Stenosis; (2) Roentgenographic Aspects of Ventricular Septal Defects, Dr. Dennison Young, New York City.

Other participants include Prof. J. H. Gaddum, Cambridge, England; Dr. William L. Howell, Washington, D. C.; Brig. Gen. Thomas W. Mattingly, Washington, D. C.; Dr. Leon Unger, Chicago. Reservations should be made by writing directly to "Bahamas Conferences," P. O. Box 4037, Fort Lauderdale, Fla.

Allergy Meeting in Chicago.—The 15th annual meeting of the American Academy of Allergy will be held at the Morrison Hotel, Chicago, Feb. 9-11 with postgraduate courses presented Feb. 7 and 8. Seventeen round-table discussions will be conducted Feb. 8, 6:30 p. m. Of the 58 papers scheduled to be presented on the scientific program the following are by Canadian authors:

Cutaneous Reactions to Autologous and Non-Autologous Plasma, Drs. Samuel O. Freedman, J. Q. Bliss, J. L. Hutchison, and A. S. V. Burgen, Montreal, Quebec.
The Antigenicity of Estrone-Protein Conjugates, Dr. Bram Rose, L. Goodfriend, and A. H. Sehon, Ph.D., Montreal, Quebec.
Metabolic Studies on Asthmatic Patients Treated with Newer Steroids, Drs. Eleanor McGarry, Eleanor Venning, and Bram Rose, Montreal, Quebec.
The Effect of Ataractic and Antihistaminic Drugs on the Experimental Skin Wheal, Dr. John H. Toogood, London, Ontario.

Dr. Merle W. Moore, Portland, Ore., President, American College of Allergists, will present "More Stress on Education in Allergy," Feb. 10. Panel discussions, exhibits, and a program of social events are planned. For information write—the American Academy of Allergy, 756 N. Milwaukee St., Milwaukee 2, Wis.

Meeting on Occupational Medicine in Boston.—The 11th annual meeting of the American Academy of Occupational Medicine will be presented at the Sheraton–Plaza Hotel, Boston, Feb. 11-13, under the presidency of Dr. Ronald F. Buchan, who, with Dr. Charles C. Lund, president, Massachusetts Medical Society, will open the meeting. A discussion on "Transplantation of Normal Human Tissue—Present Status and Future" will be moderated by Dr. John P. Merrill, Boston. A field trip to the Massachusetts Institute of Technology will be conducted the afternoon of Feb. 11 under the direction of Dr. Harriet L. Hardy, of Boston. Participants include the following: Drs. Richard J. Sexton, Charleston, W. Va.; Elwood Henneman, Mark D. Altschule, Joseph E. Murray, Gustave J. Dammin, John R. Brooks, Somers H. Sturgis, Louis Weinstein, Heinrich G. Brugsch, David G. Cogan, Mary O. Amdur, Ph.D., Willem S. Frederik, Theos J. Thompson, Ph.D., Constantine Maletskos, Ph.D., and Martin Lubin, all of Boston. The annual business meeting will be held the afternoon of Feb. 12, with the annual banquet, including presentation of the academy award and the George Gehrmann Lecture, to follow at 7 p. m. A symposium on the Nuclear Reactor and Its Products will conclude the meeting.

Congress on Industrial Health in Cincinnati.—The 19th annual Congress on Industrial Health will convene in Cincinnati Feb. 16-18 at the Netherland Hilton Hotel. Three major areas of occupational health—education, research, and practice of occupational medicine—will be discussed. Sponsored by the American Medical Association Council on Industrial Health, the congress is held as a way of "furthering the development and maintenance of high medical standards in industry." The opening session Feb. 16 will be devoted to education and training in occupational health. Dr. John D. Porterfield, Washington, D. C., deputy surgeon general, U. S. Public Health Service, will speak at the annual banquet Monday evening. The Tuesday morning discussion on research in occupational health will be conducted by Dr. James H. Sterner, Rochester, New York. Poisoning resulting from industrial chemicals will be discussed Tuesday afternoon by Herbert E. Stokinger, Ph.D., Dr. A. A. Brust, and Dr. Mitchell Zavon, all of Cincinnati. A joint meeting with the Cincinnati Academy of Medicine will be held Tuesday evening when Dr. C. W. Shilling, Washington, D. C., will discuss the problem of fallout and radiation. The congress will conclude Wednesday morning with a clinical session on the practice of occupational medicine.

World Mental Health Year.—Plans for a World Mental Health Year in 1960, sponsored by 108 mental health and professional societies in 43 countries and territories, have been announced at the New York office of the World Federation for Mental Health. Following the pattern of the International Geophysical Year, the purpose of the program is "to stimulate mental health activities, including research, with a maximum of international cooperation." The federation is a nongovernmental organization which includes 29 societies in the U. S. and 79 in 42 other countries. Five major mental health objectives have been singled out for the World Mental Health Year:

1. To increase the study of child development in different countries.
2. To increase the knowledge of the many causes and the distribution of mental illness.

3. To improve and extend the teaching of the principles of mental health in medical and nursing schools, teacher-training colleges, schools of social work, theological seminaries, and similar centers of professional training.
4. To develop knowledge and techniques for dealing with the human relations problems which arise in industries and all types of occupation.
5. To encourage the study and creation of better methods of preventing and dealing with psychological problems arising from migration within and between countries, whether voluntary or involuntary.

The decision to designate 1960 as the First World Mental Health Year was taken by the executive board of the World Federation at its annual meeting at Copenhagen, August, 1957. Responsibility for financial support of plans and projects within the United States has been assumed by the World Federation for Mental Health: United States Committee, Inc.

Meeting of Orthopsychiatrists in San Francisco.—The 36th annual meeting of the American Orthopsychiatric Association will be held at the Sheraton Palace Hotel, San Francisco, March 30-31. This will be the first West Coast meeting of the association, which brings together the disciplines involved in the team approach to prevention and treatment of behavior problems and related training and research. A presidential session on the evening of March 30 will include addresses by Dr. Linus C. Pauling, Nobel laureate in chemistry and professor of chemistry, California Institute of Technology, and Weston LaBarre, Ph.D., associate professor of sociology and anthropology, Duke University, Durham, N. C. The presidential address will be delivered by Dr. Stanislaus A. Szurek, professor of psychiatry, University of California Medical School, and director of children's services, Langley Porter Neuropsychiatric Institute, San Francisco. About 60 scientific papers and 40 workshop sessions are planned, with emphasis on social and cultural aspects of mental health, treatment methods, and research. An all-day symposium is planned on brain and behavior, with the morning discussion centering on neuropsychiatry and neurochemistry and the afternoon on psychodynamic and social factors in brain damage. Four sessions are planned to include mental health films and their discussion. Exhibits related to the practice of orthopsychiatry will be on display. Information is available from Marion F. Langer, Ph.D., Executive Secretary, American Orthopsychiatric Association, 1790 Broadway, New York 19, or from the Chairman of the San Francisco arrangements committee, Dr. Donald A. Shaskan, Veterans Administration, 49 Fourth, San Francisco 3.

Papers Wanted for Congress on Industrial Health.—The Scientific Program Committee invites submission of papers for presentation at the 13th International Congress on Occupational Health in New York City at the Waldorf Astoria Hotel, July 25-29, 1960. The program will be devoted to the following aspects of occupational health:

1. Administrative Practices.
2. Medical Practices.
3. Surgical Practices.
4. Education and Training.
5. Social and Legal Aspects.
6. Environmental Hygiene.
7. Influence of Environmental Factors in Health.
8. Work Physiology and Psychology.
9. Specific Industries.
10. General.

The official languages of the congress will be English, French, German, and Spanish. However, papers may be read in the language desired by the author. Those desiring to present papers must submit abstracts (not more than 200 words, typed double-space) before Jan. 1, 1960, to Dr. Irving R. Tabershaw, Chairman of the Scientific Program Committee, 375 Park Ave., New York City. Original contributions rather than a review of previously published material will be given priority. Three copies in English are required for use by the committee and one copy in another official language of the congress. The names, academic degrees, titles, and complete addresses of author and coauthor must be included in each abstract. The author who is to present the paper should be the first listed in the abstract. Complete texts of the papers in any one of the official languages must be submitted not later than April 1, 1960. The time allotted for each paper will be limited to 15 minutes, including slides. Complete papers will be published in the Proceedings of the congress.

Three Physicians Named "Outstanding Young Men."—The selection of America's Ten Outstanding Young Men of 1958 has been announced by the United States Junior Chamber of Commerce. The 10 men, all below the age of 36, were presented the silver "Jayson," symbolic of their selection by U. S. Jaycee president Robert V. Cox at Fort Lauderdale, Fla., Jan. 17. Included are three physicians: (1) Dr. James T. Grace, Jr., who reportedly described and confirmed the thesis that cancer patients retain a resistance to their tumors even when the disease becomes advanced. He conducts research at Roswell Park Memorial Institute in Buffalo, N. Y. (2) Dr. Richard T. Smith, who has made discoveries in the field of natural immunity and immunological tolerance in the newborn period of life. He is chief of pediatric services at the J. Hillis Miller Health Center, University of Florida, Gainesville. (3) Dr. Hugh E. Wilson, III, who is chairman of the division of cardiac and thoracic surgery and assistant professor of surgery at the University of Texas' Southwestern Medical School, Dallas. During the past two years, Dr.

Wilson reportedly played a leading part in building a cardiac research laboratory. Others named in the "Outstanding Young Men" group are: Lt. Shephard M. Jenks, navigator of the Nautilus submarine; Henry A. Kissinger, whose book, "Nuclear Weapons and Foreign Policy," was cited by the Overseas Press Club and awarded the Woodrow Wilson Prize; Pat Boone, singer-actor, who, while making recordings, television shows, and movies, earned a degree magna cum laude from Columbia University, New York City; Donald A. Glaser, professor of physics at the University of Michigan, Ann Arbor, who is the inventor of the bubble chamber; Warren H. Phillips, managing editor of the *Wall Street Journal;* Loran Edward Schnack, county and probate judge of Adams County, Ill.; and Gus Turbeville, president, Northland College, Ashland, Wis.

Standardization of Anesthesia Equipment.—The American Standards Association has announced that Anglo-American meetings were held in December to further the development of common standards for anesthesia and resuscitating equipment so as to make components of this equipment interchangeable in the two countries. Other nations reportedly have indicated that if the British and Americans can reach agreement, they would adopt the same standards. The six-man British delegation, representing the British Standards Institution, was headed by Dr. R. W. Cope, consultant anesthetist, University College Hospital, London, England. Leading the 30-man American delegation was Dr. Hamilton S. Davis, department of anesthesiology, Western Reserve University School of Medicine, Cleveland. Dr. Davis is chairman of the American Standards Association Sectional Committee Z79, which during the past three years has been working on standards for anesthesia equipment in this country under the sponsorship of the American Society of Anesthesiologists. Manufacturers of anesthesia equipment were represented on both delegations. Representatives of the U. S. Army, Navy, and Air Force, American Hospital Association, American Association of Nurse Anesthetists, and the Veterans Administration also participated. The manufacturers agreed to design prototype fittings, adapters, and connectors suitable for international standardization and to subject these parts within the next few months to field trials in the U. S. and Great Britain. The British, who have already tentative standards on these components, agreed to postpone formal promulgation of the standards until May, 1959, to await the outcome of these tests. Agreements made in England in July, 1958, on details of the proposed American standard for endotracheal tubes and cuffs were ratified at the meeting. This standard is essentially identical with the British proposal. The World Federation of Societies of Anesthesiologists was represented by its secretary, Dr. G. S. W. Organe, of Westminster Hospital, London.

LATIN AMERICA

Psychiatric Institute in Haiti.—The Haiti Psychiatric Institute, reportedly the first hospital in which treatment of the mentally ill will be based primarily on drug therapy, will begin operation in February, Dr. Nathan S. Kline, director of research, Rockland State Hospital, Orangeburg, N. Y., has announced. Located in Port-au-Prince, Haiti, it will be under the direction of Dr. Louis Mars, psychiatrist and minister of foreign affairs for the country of Haiti. The project is being financed by three pharmaceutical companies: Schering Corporation, Bloomfield, N. J.; Hoffmann–La Roche, Inc., Nutley, N. J.; Wyeth International, Radnor, Pa., and the Haitian government. It will be carried out under the auspices of MEDICO (Medical International Cooperation), the government of Haiti, and the Department of Mental Hygiene of the State of New York. Dr. Kline will serve as consultant to the Haitian program. In addition to financial grants to the project, the companies will provide the primary drugs to be used. Funds supplied by these companies are being used for the building of the clinic in Haiti, consisting of two wards of 10 beds each, and out-patient department, and other laboratory and administrative facilities. The government of Haiti is furnishing the land and operational funds for the project. In addition to scientific records, a sound motion picture is being made by MEDICO. For information contact: Mr. John Heyman, Coordinator, Rockland State Hospital, Orangeburg, N. Y.

FOREIGN

International Congress on Plastic Surgery.—The British Association of Plastic Surgeons is holding an international congress in London July 12-17. Subjects to be discussed include: Surgery of Congenital Deformities, Trauma of the Face, Surgery of Skin Cancer, Cosmetic Surgery, Industrial Injuries to the Hand, Anesthesia in Plastic Surgery, and Research Projects. Information may be obtained from the Organizing Secretary, Mr. David Matthews, International Congress on Plastic Surgery, c/o Institute of Child Health, Hospital for Sick Children, Great Ormond St., London, W. C. 1, England.

Congress on Fertility in Amsterdam.—The third World Congress on Fertility and Sterility, sponsored by the International Fertility Association, will be held in Amsterdam, Holland, June 7-13. The general outlines of the sections on the program will be as follows:

1. Female sterility (physiology of reproduction, pathology, endocrinology, clinical problems, treatment).
2. Male sterility (physiology of reproduction, pathology, endocrinology, clinical problems, treatment).
3. Basic research or animal reproduction.
4. Psychosexual problems.

Priority has been given to papers concerning the following subjects: embryonic death, hormonal factors and vitamins in fertility and sterility, relative value of the techniques for study of the endocrine functions in human sterility, biochemistry of spermatogenesis, and psychosexual problems in sterility. The official languages are English, German, Spanish (with simultaneous translation). Registration fee is $50 for a full member. For information and registration apply to Dr. L. I. Swaab, Honorary Secretary, Third World Congress on Fertility and Sterility, Sint Agnietenstraat 4, Amsterdam-C, Holland.

CORRECTION

Radiation Damage.—In the Foreign Letter entitled "Radiation Damages in Japanese Children" in the Jan. 3, 1959, issue of THE JOURNAL, page 62, all references to miles should have been to meters.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Phoenix, April 5-10. All applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the South and Southwest, New Orleans, Feb. 3-6. Final date for filing application was Jan. 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application is Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *I. Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Deadline for receipt of new and reopened application for the 1960 examinations is Aug. 1, 1959. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Philadelphia, June 2; St. Louis, Oct. 6-10. Sec., Dr. Merrill J. King, 22 White St., Rockland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* Washington, D. C., Denver, Colorado and Rochester, Minn., Mar. 26-27. Deadline for filing application was Nov. 30. *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 5-9. Final date for filing application is February. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Boston, April 16-19. Final date for filing application is Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application is February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Boston, May 9-11. Final date for submitting case reports is Jan. 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Written. Public Health.* Regional, Apr. 9-11. *Occupational Medicine.* Chicago, Apr. 17-19. *Aviation Medicine.* Los Angeles, Apr. 24-26. Final date for filing application for all three examinations is Jan. 15. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written.* Philadelphia, September. Final date for filing application is March. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New Orleans, Mar. 16-17; Chicago, Oct. 19-20; New York, Dec. 14-15. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application was Nov. 1. *Examination.* Chicago, June 2-4. If needed a special examination will be offered at this time in Nuclear Medicine to diplomates in Radiology or Therapeutic Radiology. The deadline for filing applications is April 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: *Oral.* Los Angeles, April. Final date for filing application is Dec. 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

AMERICAN BOARD OF UROLOGY: The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

AIR FORCE

Personal.—At the 125th meeting of the American Association for the Advancement of Science in Washington, D. C., in December, Col. Paul A. Campbell, Chief of the Division of Space Medicine at Randolph Air Force Base, served as chairman of a joint session of the American Physiological Society and the American Astronautical Society. Among the subjects discussed at this session were: "Man-Machine Systems in Space Vehicles," "Protection of Man Against Transient Exposure to High Heat Loads," "Psychological Research on the Environment of Outer Space," and "A Comparison of Artificial Environments Used in Sealed Cabins During Flight into the Stratosphere." At the same meeting Lieut. Col. John D. Fulton, head of the school's Department of Microbiology-Cellular Biology, delivered a paper on the survival of tiny earth organisms in a simulated Martian environment. It described the colonel's work, which was carried on at the School of Aviation Medicine since 1957. In a collection of Brewer jars, the scientist simulated both soil and atmospheric conditions thought to be identical to those on Mars. Certain types of soil bacteria, placed in the jars and carefully watched over an extended period of time, survived. The project is being expanded to include such higher life forms as moss, lichens, and algae.

NAVY

Dr. Karsner Honored.—At the annual meeting of the New York Academy of Sciences in December, the title of Fellow of the New York Academy of Sciences was conferred on Dr. Howard T. Karsner, Medical Research Advisor to the Navy surgeon general. Election to Fellowship in the Academy is an honor, conferred on a limited number of members, who, in the estimation of the council, have done outstanding work toward the advancement of science.

Course in Ophthalmic Pathology.—A postgraduate course in ophthalmic pathology will convene at the Armed Forces Institute of Pathology, Washington, D. C., from March 9-13, 1959. This course will consist of a basic and comprehensive survey of pathological conditions affecting the eye. The subjects will include a review of the normal histology of the eye, changes incident to growth and aging; a review of general inflammation; acute, chronic, and granulomatous lesions and their sequelae; injuries; cataract; glaucoma; vascular diseases; intraocular tumors; and epibulbar and orbital inflammatory and neoplastic lesions. Applications from medical department officers on active or inactive duty will be forwarded through channels to the Chief, Bureau of Medicine and Surgery, Department of the Navy, Washington 25, D. C., six weeks prior to the opening date of the course. Priority will be given to officers who are board certified or board qualified, or to residents in a specialty related to the course desired.

PUBLIC HEALTH SERVICE

Examinations for Commission.—Competitive examinations for appointment to the commissioned corps of the United States Public Health Service will be held throughout the nation for physicians, April 21, 22, 23, and 24. Applications for these examinations must be filed with the surgeon general no later than March 6. Application forms and further information may be obtained by writing to the Surgeon General, U. S. Public Health Service, Washington 25, D. C. The examinations are customarily held at the Public Health Service installation nearest the applicant's home, school, or place of business. The time and place of the examinations will be announced to all applicants well in advance of the examination dates. To be eligible for appointment to the regular corps of the Public Health Service, candidates must be United States citizens, graduates of approved schools, and at least 21 years of age. Applicants who expect to meet these basic entrance requirements within nine months from the date of the written examination of choice may take the examination, but they will not be appointed to the regular corps until they have fulfilled all other requirements.

Candidates who successfully pass the entrance examination will be appointed in the grade of either the assistant or senior assistant (equivalent to Navy lieutenant, j. g., and lieutenant, or Army first lieutenant and captain). Public Health Service officers receive the pay and allowances of officers of equivalent grade in the Army, Navy, and Air Force and share many of the same benefits and privileges. Medical officers receive an extra $1,200 to $3,000 a year in incentive pay. Active duty service as a Public Health Service officer, moreover, is sufficient to satisfy Selective Service obligations under the Universal Military Training and Service Act.

DEATHS

Fenton, Ralph Albert Ⓜ Portland, Ore.; born in Lafayette, Nov. 5, 1880; Northwestern University Medical School, Chicago, 1906; since 1946 professor emeritus of otolaryngology at the University of Oregon Medical School, where he joined the faculty in 1911, and where in 1927 he became professor and head of the department of otolaryngology; member of the House of Delegates from 1932 to 1935, and chairman, Section on Laryngology, Otology and Rhinology of the American Medical Association in 1935-1936, and the following year became a member of its Board of Trustees serving until 1942; member, past-president, and vice-president of the American Laryngological Association which in 1944 awarded him its De Roaldes prize and in 1928 shared with Olaf Larsell, . Ph.D., its Casselberry prize; past-president, vice-president, and secretary of the Pacific Coast Oto-Ophthalmological Society; past-president of the Portland Academy of Medicine, and Oregon Academy of Ophthalmology and Otolaryngology; member and past-vice-president of the American Academy of Ophthalmology and Otolaryngology, of which he was at one time secretary; member of the American Laryngological, Rhinological and Otological Society and from 1926 to 1930 Oregon councilor; member of the American Otological Society, Association of Military Surgeons of the United States, Chi Psi, Aero Medical Association, Nu Sigma Nu, Phi Beta Kappa, Sigma Xi, and Alpha Omega Alpha; in 1931 United States delegate to the International Congress on Military Medicine and Pharmacy at The Hague; head of the Portland chapter of the Military Order of the World War I; during World War I went overseas as a major in Base Hospital 46, serving in many of the same sectors of France as the famed 91st division; served in the Army of Occupation in Germany and rose to the rank of colonel in the Army Reserves; served as a member and director of the American Board of Otolaryngology; specialist certified by the American Board of Ophthalmology; a director of the Multnomah County Library Association from 1926 to 1953; was named for a second four-year term on the state commission for the blind in 1939 and was chosen a regent of Reed College in 1936; served on the staffs of St. Vincent's, Physicians and Surgeons, and Multnomah County hospitals, Portland Sanitarium, and Doernbecher Memorial Hospital for Children; consultant in otolaryngology to the Veterans Administration Hospital; received an honorary doctor of science degree from the University of Oregon in 1943; recently Dr. Fenton became a member of the advisory committee to the Sommer Memorial Lecture Fund endowed by the late Ernst A. Sommer of Portland for the advancement of postgraduate medical education in the Pacific Northwest; member of the editorial board of *A. M. A. Archives of Otolaryngology;* died Nov. 2, aged 77.

Ernest Edward Irons, M.D., 1877–1958.

Irons, Ernest Edward Ⓜ Chicago, President of the American Medical Association, 1949-1950, died in the Presbyterian Hospital Jan. 18, aged 81. Dr. Irons was born in Council Bluffs, Iowa, Feb. 17, 1877. He obtained his bachelor of science degree at the University of Chicago in 1900 and his doctor of medicine from Rush Medical College, Chicago, in 1903. He was awarded the degree of doctor of philosophy for research from the University of Chicago in 1912. Since 1903 he practiced in Chicago. From 1902 to 1904 he was assistant in pathology and bacteriology at the University of Chicago, under Professor E. O. Jordan. Early in his career he became associated with the Presbyterian Hospital in Chicago. From 1923 to 1936 he was dean of students and dean of the faculty of his alma mater, where for many years he was clinical professor of medicine and chairman of the department. Since 1941 he held the title of (Rush) clinical professor emeritus at the University of Illinois College of Medicine. In 1939 the Kappa Chapter of the Nu Sigma Nu Fraternity at Rush Medical College and at the University of Chicago established an annual lecture in his honor. In 1940 he gave the Charles R. Bardeen Memorial Lecture at the University of Wisconsin Medical School. Dr. Irons was elected to membership on the Council on Pharmacy and Chemistry of the American Medical Association in 1923, and served for 18 years. In 1929-1930 he was chairman of its Section on the Practice of Medicine and from 1940 to 1948 he was a Trustee. Following the death of Dr. Austin A.

Ⓜ Indicates Member of the American Medical Association.

Hayden, Dr. Irons was elected to fill the unexpired term as secretary of the Board of Trustees. In 1941 he was elected secretary of the board, serving until 1948 when he was chosen President-elect. He was a representative of the American Medical Association in the World Medical Association. He was an exregent of the American College of Physicians, and in 1945 president, president of the American Association for the Study and Control of Rheumatic Diseases in 1934, of the Society of Medical History of Chicago in 1940, and of the Institute of Medicine of Chicago in 1946. He was a member of the American Board of Internal Medicine, the American Rheumatism Association, Association of American Physicians, Central Society for Clinical Research, American Society for Clinical Investigation, and the American Association of Pathologists and Bacteriologists. In World War I he became colonel in command of the Base Hospital at Camp Custer near Battle Creek, Mich., and during World War II he represented medicine in many different capacities including several important committees of the National Research Council. In 1947-1948 he traveled abroad for the United States government to study health conditions. He went to Japan to recommend changes in that country's health programs for the post World War II occupation administration of Gen. Douglas MacArthur. He also made a study of medical practice in Puerto Rico. Dr. Irons was appointed by Mayor Kennelley of Chicago to the board of directors of the City of Chicago Municipal Tuberculosis Sanitarium and he became president of the board. He was consulting physician at the Presbyterian Hospital. In 1946 he was awarded the "Goldheaded Cane" of the School of Medicine of the University of California, held also by Dr. James B. Herrick, Chicago, with whom he had been associated many years. In 1958 he was presented the Chicago Medal of Merit for his contributions to the city, and the first annual Tuberculosis Institute medal in 1958 for outstanding work in the field. Distinguished for his contributions in medical research, especially in focal infection, iritis and rheumatic diseases, Dr. Irons was accorded many honors by the medical profession. His recent writings on medical economics and social medicine have been extensive and authoritative.

Johnson, Herbert William, Gorham, N. H.; Harvard Medical School, Boston, 1906; served as Gorham selectman for six years and for 27 years was an officer of the District Nurses' Association; served on the Park Commission for seven years; on the staff of St. Louis Hospital in Berlin; died Oct. 31, aged 79.

Johnson, Herman Walter Ⓜ Buffalo, N. Y.; born in Andover, Vt., Aug. 2, 1883; University of Buffalo School of Medicine, 1905; served as professor of obstetrics and chairman of the department at Baylor University College of Medicine in Houston, Texas; specialist certified by the American Board of Obstetrics and Gynecology; member of the American Association of Obstetricians and Gynecologists and the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; served overseas during World War I; formerly on the consulting staff, Memorial and Herman hospitals, on the honorary staff, St. Joseph's Infirmary, and obstetrician and gynecologist-in-chief at the Jefferson Davis Hospital and the Methodist Hospital in Houston; died Nov. 13, aged 75.

Landi, Oscarre Ⓜ New York City; Regia Universita di Torino, Facolta di Medicine e Chirurgia, Italy, 1927; specialist certified by the American Board of Dermatology and Syphilology; served on the staffs of the Hospital for Joint Diseases and Mount Sinai Hospital, where he died Nov. 10, aged 55.

Pope, Emma Wightman, Carmel, Calif.; Medical Department of the University of California, San Francisco, 1899; an associate member of the American Medical Association; served as secretary of the California Medical Association; died in the Peninsula Community Hospital Nov. 1, aged 87.

Shortridge, Wilbur Holmes Ⓜ Seymour, Ind.; Indiana University School of Medicine, Indianapolis, 1935; from 1953 to 1955 a lieutenant commander in the U. S. Naval Reserve and one year aboard the USS Ajax in Far East; on the staff of the Jackson County Schneck Memorial Hospital; died Oct. 28, aged 52.

Skaggs, David Goodson, Prospect, Ky.; Hospital College of Medicine, Louisville, 1902; died in the Kentucky Baptist Hospital, Louisville, Oct. 23, aged 82.

Thomas, J. Orville Ⓜ North Branch, Mich.; Detroit College of Medicine, 1897; in June, 1949, a "Dr. Thomas Day" was held to honor him for his services; died in the Samaritan Hospital, Bay City, Oct. 20, aged 81.

Tippin, Ernest Elwood Sr. Ⓜ Wichita, Kan.; Rush Medical College, Chicago, 1920; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the American Society of Ophthalmologic and Otolaryngologic Allergy; veteran of World War I; associated with St. Francis and Wesley hospitals; died Oct. 30, aged 68.

Trentzsch, Max William, Highland, Wis.; University of Illinois College of Medicine, Chicago, 1913; died Oct. 29, aged 77.

Williams, Leon Arlington Ⓜ Minneapolis; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1897; died in Lester Prairie Oct. 15, aged 86.

FOREIGN LETTERS

AUSTRIA

Diagnosis of Operable Cardiac Defects.—At the meeting of the Society of Physicians in Vienna on Nov. 21, Dr. F. Grosse-Brockhoff stated that such diagnostic methods as cardiac catheterization, angiocardiography, retrograde aortography, and puncture of the left atrium and left ventricle made it possible to more accurately evaluate the significance of the symptoms. Pulmonary stenosis, aortic stenosis, patent ductus arteriosus, and tricuspid stenosis can be diagnosed with a high degree of probability by such bloodless methods as inspection, palpation, auscultation, phonocardiography, roentgenography, electrocardiography, and ultrasonic echo waves. Even if further examination with more radical and technically more complicated methods is necessary to establish the diagnosis before an operation as is the case in patients with congenital cardiac defects, the clinical diagnosis should be very much in the foreground.

Liver Function Tests.—At the same meeting Drs. R. Boller and H. Partilla said that the galactose tolerance test may yield different results, depending on whether it is performed at the usual time in the morning or whether it is started at 3 a.m. These differences depend on the condition of the patient's liver. This has a diagnostic and a prognostic significance. Patients with mild forms of hepatic diseases show lower galactose excretion if the test is started at 3 a.m. rather than at the usual hour, whereas patients with severe forms of hepatic diseases show a higher galactose excretion in the nocturnal than in the diurnal test. If serial tests are made for longer periods on patients with liver disease who show higher galactose excretion during the night compared to the day, it can be seen that even before the patients show clinical signs of improvement there is a change in the test reaction, in that the excretion of galactose during the night test decreases, whereas it increases during the day. In patients in whom the disease progresses, no such change in reaction is observed. If patients with hepatitis are treated with prednisone, a higher galactose excretion in the night is expected in those in whom prednisone has a therapeutic effect. A prompt reaction in the galactose excretion can be observed in those patients. In other words, in patients who respond to prednisone, a lower galactose excretion is expected in the nocturnal test than in the diurnal test or both tests show a negative result. The behavior of these galactose tests started at different times of the day has its explanation in the day and night rhythm.

Escape of Cerebrospinal Fluid from the Nose.—At the meeting of the Society of Physicians in Vienna on Nov. 14, Dr. D. W. Krüger stated that posttraumatic escape of cerebrospinal fluid from the nose in the early as well as the late stage should be treated surgically. In four patients escape of cerebrospinal fluid from the nose occurred after a nasal operation, due probably to a congenital defect in the lamina cribrosa. The surgical approach is mainly intradural and the defect in the lamina cribrosa may be covered with strips of fascia after the ethmoid sinuses have been evacuated and supplied with a muscle tampon. Dr. E. Wodak said that rhinologists may see patients with cerebrospinal fluid escaping from the nose after frontobasal injuries. They agree that a reparative operation should be performed if the escape of cerebrospinal fluid does not cease within a few days. Often it becomes evident that bone injuries are more diffuse than the roentgenograms indicate and the clinical findings may be obscured by giving antibiotics. The approach in patients with recent injuries is extradural. The laceration of the dura mater is closed after bony fragments have been removed. The case of a 13-year-old boy showed how important this operation is. The boy fell from a tree and did not present any symptoms. He was afebrile but had a cerebrospinal fistula. At operation, in addition to multiple fractures, a large frontal cerebral abscess was found.

JAPAN

Poliomyelitis and Salk Vaccine.—Japan is now importing Salk vaccine from the United States. The government has started to manufacture this vaccine in a pilot plant but will not be able to meet the ever-increasing demand before 1960. The incidence of poliomyelitis has practically doubled since last year. Over 2,486 cases were reported in the first 11 months of 1958.

Tuberculosis.—According to a government report, about 1 person in every 300 is actively tuberculous. About 50% of all available hospital beds are occupied by tuberculous patients. The worst aspect of the situation is that more than one-half of the very sick are not receiving proper medical attention. Although the death rate has decreased mark-

The items in these letters are contributed by regular correspondents in the various foreign countries.

edly in the last 10 years, the number of active cases has increased by about 120,000 in the past 5 years. The reduction in the death rate, effected by the use of modern treatment methods, has occurred chiefly in the age group 20 to 24. As in some other countries, a large scale shift in incidence from youth to middle age has taken place. This may be accounted for in Japan by the following facts: Since 1951 all school children ranging in age from 6 to 15 years were examined annually. All those who had a negative reaction to tuberculin tests were given BCG vaccine and all those who had a positive reaction were x-rayed. In 1955 the basic plan of tuberculosis control was revamped to include all ages instead of being limited to those under 30.

PORTUGAL

Aspergillosis.—Cortez Pimental (*Gazeta médica portuguesa* 11:455-471, 1958) reported four new cases of pulmonary aspergillosis. The main phases of this type of aspergillosis are presence of an aspergillar mass within a preexisting cavity, atrophy and erosion of the epithelium at the level of the regions in close contact with the fungus mass, formation of a granulation tissue and its extension into the cavity, production of foreign body giant cells, and reabsorption of the micellar masses. At variance with former opinions, the author does not consider the Aspergillus as harmless, but on the other hand, he does not admit its invading properties. Its presence in the pulmonary cavity originates a pathological process similar to that caused by an intrabronchial body. Such process has a tendency to progress due to its constant growth, size, and frequency of association with secondary infection.

UNITED KINGDOM

Increase in Crime.—Mr. Butler, the Home Secretary, told the House of Commons that crime has increased by 50% in the last 20 years, the increase being greatest in the last 3 years. The chief offenders were youths between 16 and 21 years of age. There has recently been an increase in offenses committed by persons under 17. Mr. Butler said that a new research unit has been established in the Home Office for the investigation of crime and that an Institute of Criminology would soon be operating at Cambridge. The Institute for the Scientific Treatment of Delinquency also promoted scientific research into the causes and prevention of crime. This is timely, as corrective methods do not appear to prevent the increase in the number of young criminals. The clinical work of the Institute for the Scientific Treatment of Delinquency was taken over by the National Health Service 10 years ago. Its main activities are research, education, and the publication of the *British Journal of Delinquency*. The educational program is based on the view that crime is a form of behavioral disorder to be correlated with other social and psychological disorders and treated along similar lines.

Royal Commission on Doctors' Pay.—Further evidence to the Royal Commission on Doctors' and Dentists' Remuneration has been given by the Joint Consultants Committee. It suggested that the salaries of hospital medical staff should be increased by 29% to offset the fall in the value of money in the last six years and to maintain the economic standards of physicians in relation to other professions. It also recommended that the so-called distinction awards given to the top hospital consultants should be increased by 60%. If implemented, this would give an intern a salary of $1,550 a year, a consultant on the basic scale $7,600 to $11,200, and a consultant receiving the top merit award $17,800 to $22,400. The memorandum drew attention to the alarmingly high proportion of physicians attracted by prospects overseas, who are now emigrating. This in itself suggests that conditions in the National Health Service are not satisfactory. Young physicians emigrate because they object to working in a state monopoly and because financial prospects are better abroad. In one area the rate of emigration was 5 per 1,000 per year, and not all these physicians were young. Mr. Holmes Sellors, a member of the committee, referred to what he called the "inverted Micawberism" of the health service—"they are always waiting for something to turn down, rather than something to turn up."

Tuberculosis in Animals.—The danger of the dissemination of tuberculosis by domestic animals was emphasized by Dr. Soltys (*Brit. M. J.* 2:1133, 1958). There are over 10 million cattle in Great Britain and only 73% are tuberculin negative. Tubercle bacilli readily gain access to the milk, particularly if the udder is infected. Of 570 samples of milk examined by the Veterinary Investigation Center, Cambridge, 72 or nearly 13% contained tubercle bacilli. In spite of the great advances in the control of tuberculosis in cattle there will be a constant potential hazard so long as any infected animals exist. It has been proved that persons with open tuberculosis can infect cattle with the human type of baccillus. In all probability horses, sheep, and goats are not a source of danger to man, as the incidence of tuberculosis in these animals is low, but 10 to 15% of pigs in Britain are infected. The poor sanitary conditions in some slaughterhouses, and the handling of meat and organs of tuberculous animals, present a serious risk of infection for meat inspectors and slaughterhouse employees. The public health aspect of tuberculosis in dogs and cats should receive closer attention, because cats can be infected from cow's milk and dogs by contact with human cases. These animals are in close proximity to their owners and particularly to children. At present the control and prevention of animal tuber-

culosis is vested in the Ministry of Agriculture. All questions referring to animal diseases in relation to human health are dealt with by the Ministry of Health, but neither ministry employs a veterinarian as an advisor on veterinary matters affecting public health, as is done in some other countries.

Doctors' Hobbies.—The second Doctors' Hobbies Exhibition was opened on Nov. 10 at British Medical Association House in London. There were more than 700 exhibits by 500 physicians. The first prize ($210) was won by Dr. A. W. Fawcett, a thoracic surgeon, who exhibited a four-foot model of the torpedo-boat destroyer, Tigress, in which he once served, and which took 14 years to construct. The model has miniature recoil guns, a capstan, navigation lights, and davits to lower the lifeboats, all of which can be operated electrically. The second prize ($140) went to Dr. A. H. Wortman for a collection of stamps issued by Imperial Russia in 1858. Dr. S. Compton won the third prize ($70) for his tapestry work. An interesting exhibit was a telephone wire-tapping device, the work of Dr. Michael Ball of the Royal Air Force. He referred to this as an illegal invention and said he would not patent it, or divulge its construction, in case it fell into unscrupulous hands. The most popular exhibits dealt with photography and oil and watercolor paintings, followed by embroidery, woodwork, wood carving, and sculpture. A copy of a Stradivarius violin by Mr. Eric Peet, of the department of plastic surgery, Oxford, took 200 hours to make and was rated the best exhibit in the woodwork section. Dr. Hamilton showed a collection of 40,000 rail tickets from all over the world, including tickets to Hell and Paradise. A former vice-president of the Royal College of Surgeons, Mr. Lawrence Abel, exhibited some barber surgeons' bowls, including a Chinese one dated 1450. The exhibits covered a wide range, including a pair of tame chinchillas, popular songs, stage properties, poetry, an electronic organ, model trains and ships, ceramics, ships in bottles, and matchbox labels.

Environment and Blood Pressure.—The effect of environment on blood pressure was studied by Miall and Oldham in population samples from Rhondda Fach, a mining village in Wales, and from the Vale of Glamorgan, an agricultural area (*Clin. Sc.* **17**:409, 1958). Samples chosen at random were assumed to be representative of the general population in the two districts, with their strikingly different environments. By standardizing blood pressures for age and sex, they found that a number of environmental factors have a marked influence on arterial pressure. Occupation, either directly or indirectly through economic circumstances, was found to affect it. Those in light occupations, with higher incomes, higher standards of living, and a lower energy expenditure were observed to have higher pressures than did heavy manual workers with higher expenditure of energy, lower incomes, and lower living standards. There was a steady gradation between the two extremes of activity and income. The differences were not due to differences in arm girth or weight. The effects of occupation were most noticeable in bachelors and men over 50. These were the two groups of people who most truly reflected occupational differences in income and energy expenditure. An inverse correlation was found with family size; the larger the family, the lower the blood pressure. This was true of the men as well as the married women. Single men had higher systolic pressures than did married men, and the fathers of small families had higher pressures than those of large families. This influence of family size became less obvious in elderly persons.

Typhoid from Oysters.—Six cases of typhoid reported in London have been traced to the eating of infected oysters from West Mersey, Essex. The port authority medical officer stated that the oyster fisherman must either submit their catches to bacteriological control before marketing or have a closing order issued. Many of the oysters caught in Great Britain are put through a cleansing station, and if the infection of the West Mersey oysters continues a station may be set up there. The possibility of infrared sterilization of the oysters is being considered.

Testing Rubber Gloves.—Although rubber gloves are frequently tested for perforations, this is seldom done after sterilization and never while in actual use. Small perforations are a potential source of postoperative infection, especially with staphylococci which may be present in the sweat of the surgeon's hand. Penikett and Gorrill have devised a method for testing the integrity of rubber gloves while on the operator's hands without impairing their sterility (*Lancet* **2**:1042, 1958). The method is based on the insulating properties of rubber. An electrical circuit is provided with two terminals, one a pad of moistened cotton gauze, the other a heat-sterilized stainless steel bowl containing a mixture of sterile saline solution and 1% chlorhexidine solution. To test a glove, contact is made between the skin of the forehead and the gauze pad, and then each gloved hand is dipped vertically into the bowl. If there is a perforation a current flows between the two electrodes because fluid enters the perforation and robs the glove of its insulating properties. The current can be made to operate a buzzer or warning light. The chlorhexidine insures that any bacteria that do leak out are killed and do not infect gloves during the next test. If heavy infection is suspected the stainless steel bowl can be changed.

MISCELLANY

PUBLIC HEALTH SERVICE

Conference Urges More Poliomyelitis Vaccinations

In order to review the nation's experience with poliomyelitis during 1958 and to map out ways of promoting more vaccinations before next summer, Dr. Leroy Burney, surgeon general, U. S. Public Health Service, called a meeting in December in Washington, D. C., of 30 officials from national medical groups, voluntary health organizations, and state and local health departments.

The surgeon general urged parents of young children who have not been vaccinated, particularly those under five, to start their children on the course of three vaccinations immediately. Dr. Burney said, "It is a tragic circumstance that hundreds of children and young adults will be spending the balance of their lives in wheel chairs or on crutches because of a failure to be vaccinated. The parents of these children and all adults up through the age of 40 should also be vaccinated."

The primary conclusion of the conference was that intensive campaigns by local communities will be necessary throughout the coming months if millions of unvaccinated Americans under 40 years of age are to be protected before next summer. The conference stressed that such campaigns need to be organized on a block-by-block home-by-home basis. A special effort is needed, the conference agreed, to promote vaccination of children under five years of age, among whom more than half of the cases of paralytic poliomyelitis occurred this year, and of less advanced socioeconomic groups, among whom the percentage of vaccination is lowest.

There was general agreement that the point has been reached in most localities at which "face to face" campaigns under the leadership and active cooperation of local groups will be necessary to reach the "hard-to-get" segments of the population who have not responded to the poliomyelitis vaccination programs conducted by the National Foundation, the American Medical Association, the Public Health Service, and local organizations throughout the nation. "With 72 million Americans vaccinated with at least one shot, this has been one of the most successful health campaigns of recent years," said Dr. Edgar Martmer of Detroit, past-president of the American Pediatric Society, who represented the American Medical Association, "but now we need to finish the job."

The conferees urged health officials and medical societies at the county and community level to examine their local situations and determine the level of vaccination by age groups and other pertinent categories and attempt to pinpoint the factors that have prevented more complete vaccination of the most susceptible groups in their areas. Such surveys will help in planning and carrying out renewed efforts at further vaccinations. Specialists from the U. S. Communicable Disease Center reported that a survey was recently conducted in the city of Atlanta and offered the services of technicians to help other cities work out similar studies.

An important step forward, the conferees agreed, was a resolution passed Dec. 4 by the American Medical Association's House of Delegates, meeting in Minneapolis, which unanimously recommended that (1) each physician assume responsibility for making sure that all members of all families he sees are fully vaccinated; (2) that state medical societies work with state health departments to bring county and local medical societies together with health departments to work out vaccination programs; and (3) that county medical societies meet with local health departments to make surveys of local problems and devise ways to meet local situations.

The conference heard reports on the 1958 occurrence of poliomyelitis in the United States, including three epidemic areas: Detroit, New Jersey, and Virginia and nearby West Virginia; the latest data on efficacy of the vaccine; and the number of people already vaccinated, by age groups, geographic areas, and socioeconomic status.

PHS specialists from the Communicable Disease Center presented the following information on poliomyelitis in 1958:

1. There was more paralytic poliomyelitis in the United States in 1958 than in 1957, although considerably less than had occurred in any of the previous 15 years. Through Nov. 22 a total of 5,563 cases had been reported, of which 2,810 were paralytic. The poliomyelitis season in 1957 began in mid-June, somewhat later than usual, and persisted through October, with the peak in mid-September.

Attack rates this year were highest in one-year-old children, with more than 50% of all paralytic cases occurring in children under 5 years of age. The Communicable Disease Center said the figures showed a general pattern of outbreaks in urban areas, in incompletely vaccinated groups of children under 5 years of age, and in lower income groups, although there was still a sufficient number of cases outside these groups to justify urging vaccination of all persons under 40 years of age.

2. The vaccine continues to show a high rate of effectiveness. Only 12.7% of persons with paralytic cases in 1958 had received three shots of the vaccine. This is an effectiveness rate of about 87%.

3. Duration of immunity is also holding up well. From available data, the vaccine continues to be effective among persons who were vaccinated more than three years ago.

The meeting also heard detailed reports from health officials of the three epidemic areas, Detroit, which had 519 cases of paralytic poliomyelitis this year, the second worst epidemic in its experience; New Jersey, where three counties including Jersey City and Newark experienced an epidemic of 101 paralytic cases; and southwest Virginia and nearby West Virginia, where 146 paralytic cases occurred in a two-state area of 29 counties.

The PHS, it was agreed, will continue to offer aid in epidemics and in situations where epidemics are emerging; to study and maintain surveillance on the national problem; and to conduct a program of public information and education, including cooperative efforts with national organizations, to keep public attention focussed on the problem of poliomyelitis vaccination.

Attending the meeting were representatives of the American Medical Association, the American Academy of General Practice, the American Academy of Pediatrics, the Pharmaceutical Manufacturers Association, the National Foundation, the Advertising Council, Inc., and the National Health Council, in addition to state and local health department representatives and PHS staff members.

CORRESPONDENCE

WARNING AGAINST INTRATHECAL USE OF METHYLENE BLUE

To the Editor:—For at least 30 years methylene blue has been used by neurosurgeons as a dye to color the cerebrospinal fluid. In most instances the dye has been injected into hydrocephalic ventricles in the effort to demonstrate the presence or absence of a block somewhere within the ventricular system. Under these circumstances the dye becomes almost immediately very dilute. Emboldened by the use of the dye in this fashion, neurosurgeons have, on occasion, injected the dye directly or in diluted form into the lumbar subarachnoid space. We recently have used the dye in this fashion drawn from a 10-cc. ampul of aqueous 1% methylene blue solution as used intravenously. In our own case 1 cc. of the dye was diluted in 25 cc. of spinal fluid and was then injected. Shortly thereafter there was discomfort, and then followed a rather profound paraplegia, which fortunately cleared in the course of several weeks, but there was a residual perineal anesthesia and bladder dysfunction. Personal inquiry among neurosurgeons leads me to believe that this mishap has occurred in other hands as well. To date I have seen no publication bearing on the matter. The purpose of this letter is to offer an urgent word of warning against the intrathecal use of this substance.

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GOUT AFTER DIURIL THERAPY

To the Editor:—An article, "Chlorothiazide (Diuril) as a Hyperuricacidemic Agent," appeared in The Journal (**168:**2128-2129 [Dec. 20] 1958). I have seen two patients with typical acute gout after the initiation of chlorothiazide therapy. The serum uric acid level in each was high. In each patient there have been no recurrences for 12 and 18 months, respectively, despite maintenance doses of the drug.

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THE BIRTH AND DEATH OF SPECIALTIES

To the Editor:—Dr. Iago Galdston's paper "The Birth and Death of Specialties," which appeared on pages 2056-2061 in the Aug. 23, 1958, issue of The Journal, was read as the sixth Herman L. Reiss Memorial Lecture at the New York Academy of Medicine Building on Oct. 28, 1957, on invitation by the New York Institute of Clinical Oral Pathology. We believe that the readers of The Journal might like to have this additional information, since there was no reference to it in the footnote when the paper was published.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Glutamic Acid Treatment of Hepatic Coma: Report on 10 Patients Treated and Review of 127 Cases Reported in Literature. T. Bennike. Bibl. læger **150**:317-330 (No. 4) 1958 (In Danish) [Copenhagen].

Ten cases of hepatic coma in middle-aged or elderly patients were treated with glutamic acid. A certain improvement, usually transitory, resulted in half the cases. A possible precipitating factor was demonstrated in 4 of these patients. Of the 5 patients who did not respond to the treatment 4 were women past menopause. The 127 published cases of hepatic coma treated with glutamic acid during the last 3 years were mainly in patients with hepatic cirrhosis or subacute chronic hepatitis; only 15 had acute hepatitis. Improvement, usually transitory, occurred in less than half the number, but was seen in half the cases where the condition had probably been precipitated by exogenic factors. Glutamic acid treatment is symptomatic and directed to the neurologic manifestations of the hepatic coma. Ammonia intoxication is considered one of the factors in the pathogenesis of hepatic coma, but even in gravely comatose patients ammonia values in the blood may sometimes be normal. The increased ammonia concentration in the blood is presumably only an indication of a deep-seated disturbance in the N metabolism.

Malignant Pseudomembranous Staphylococcus Enteritis. E. Sivertssen and E. Juel. Tidsskr. norske lægefor. **78**:993-994 (Oct. 15) 1958 (In Norwegian) [Oslo].

In the Central Hospital in Trondheim a case of malignant pseudomembranous staphylococcus enteritis in a boy aged 7 with diabetes mellitus was treated successfully. The enteritis originated 3 to 4 days after the start of tetracycline treatment for bronchopneumonia. The patient's long-continued unconsciousness is attributed mainly to a toxic effect on the cerebrum. The condition of shock with brain anoxia, dehydration, and electrolyte disturbances may have played a part. The diabetes was in the main under control and the renal function was good. Treatment of malignant pseudomembranous staphylococcus enteritis must first of all be directed to terminating the condition of shock and providing adequate supply of fluid. Immediate start of treatment with a specific antibiotic is of vital importance. Most pathogenic staphylococci are still sensitive to erythromycin, but increasing resistance is reported. The staphylococci in the case described became resistant to erythromycin after a week's treatment.

The Use of Exchange Transfusion in Acute Renal Failure. R. K. Smiley. Canad. M. A. J. **79**:740-742 (Nov. 1) 1958 [Toronto, Canada].

Smiley points out that attempts to use exchange transfusion in the management of renal failure began in 1926, when Nyiri showed that cross transfusion between normal and uremic dogs would remove nitrogenous products from the uremic dogs. The first exchange transfusion in an adult was performed in France in 1947, and in 1949 Bessis recommended the exchange of the equivalent of a patient's total blood volume every 2 or 3 days in the management of renal failure. Since then the technique has been used in patients with renal failure by several French and American authors. The case reported in this paper was that of a 31-year-old woman who was hospitalized in her sixth month of pregnancy because fetal movements had not been felt for one month. Nine days after admission, the patient delivered a macerated stillborn fetus. There was no unusual bleeding and she was discharged 5 days later.

Nine days after discharge the patient was readmitted because of profuse vaginal bleeding. Dilatation and curettage of the uterus were performed at once, but bleeding continued. Continuous blood transfusions were begun, and a hysterectomy was performed. Acute renal failure with severe prolonged oliguria occurred after this patient had received 500 cc. of incompatible blood while anesthetized. The subsequent clinical course and the attendant biochemical changes were similar to those that have been described in many patients with acute renal failure of diverse etiology. The presence of decreased prothrombin activity and thrombocytopenia with a markedly prolonged bleeding time during the bleeding phase immediately after infusion of the incompatible blood was

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confirmed. Measurements of plasma fibrinogen were not made, but the coagulation time was normal and a firm clot formed.

Exchange transfusion was performed on the 15th day of oliguria when the patient's condition, characterized by coma and repeated convulsions, was judged to be desperate. These serious manifestations disappeared during the exchange procedure and did not recur although the urine output did not exceed 500 cc. until the fifth day after the exchange transfusion. After that the patient became progressively more alert. Her convalescence was slow and marked by polyuria and thirst. Five months after the episode of renal failure, the patient was asymptomatic. Routine examinations of the blood and urine revealed normal results. While the French investigators had suggested that the exchange procedure be repeated every second day in order to remove an amount of urea calculated to be equal to the amount which would be produced in 2 days, in the case reported here, the improvement was maintained throughout the subsequent days of oliguria, and so the procedure was not repeated.

SURGERY

The Patella in Degenerative Joint Disease: A Clinicopathologic Study. R. A. Haliburton and C. R. Sullivan. A. M. A. Arch. Surg. 77:677-683 (Nov.) 1958 [Chicago].

A total of 154 patellectomies were performed on 136 patients with degenerative disease of the patellofemoral joint at the Mayo Clinic between 1950 and 1954. There were 85 female and 51 male patients between the ages of 15 and 58 years. The patients complained of pain, and associated complaints were locking, instability, stiffness, crepitus, and swelling. Physical findings were tenderness, crepitus, effusion, and limitation of motion. Forty-five patients had a history of trauma, and 20 had one of recurrent dislocation of the patella. Seventy-two patients were 30 lb. (13.6 kg.) or more overweight. One hundred nineteen patellas removed from 41 male and 68 female patients (with both patellas removed from 10) were subjected to pathological examination and graded according to the degree of degenerative change. Twenty-eight patellas were classified as grade 1, i. e., cartilage degeneration with absence of or slight marginal hyperplasia; 58 patellas showed grade 2 cartilage degeneration with well-marked marginal hyperplasia, and 33 grade 3 with gross distortion in the shape of the patella, with eburnation of the articular surface. Seventy-four of the 109 patients were followed up for 2 to 7 years after the patellectomy; in general the patients were well satisfied with the results of the surgical measures, and the patients who had patellar degeneration of grade 3 were the most satisfied group.

Advanced degenerative disease of the patellofemoral joint is commoner among women than among men. The patellas of these patients are worn out on the lateral side and have a characteristic appearance. The higher incidence among women is probably the result of increased tendency for the patella to displace laterally, either from dysplasia of the joint or from the more acute valgus alignment of the knee in women. Patellectomy for degenerative joint disease gives subjective improvement in a high proportion of patients, particularly those with advanced disease.

Extrapleural Pneumolysis and Pulmonary Tuberculosis: Preliminary Hospital Results in a Series of 200 Cases. G. G. I. Gordon. East African M. J. 35:527-532 (Sept.) 1958 [Nairobi, Kenya].

The author reports on 200 consecutive patients, between the ages of 12 and 74 years, who underwent extrapleural pneumolysis for pulmonary tuberculosis and were followed up postoperatively for periods varying from a few months to about 2½ years. In general, the operation was performed on patients with disease severely affecting the upper lobe, with or without lesions in other areas. The relative indications were failure of antibiotic therapy, failure of artificial pneumothorax or pneumoperitoneum, and persistent hemoptysis when uncontrolled by other measures. Full antibiotic cover was considered essential, both during and after the surgical intervention. Surgical complications were as follows: Marked hemorrhage into the extrapleural space, requiring blood transfusion, occurred in 7 patients; severe surgical emphysema occurred in 6 patients, contralateral spread in 6 patients, air embolism in 5 patients, tuberculous infection of the extrapleural space in 5, pyogenic infection of the space in 4, and serious mental symptoms in 2. Eleven patients died, representing an operative mortality of 5.5%. Death resulted from air embolism in 3 patients, from anesthesia in 2, from respiratory failure in 2, from tuberculous empyema in 2, from pulmonary embolism in 1, and from hemoptysis in 1. Considering the fact that most of the patients had extensive pulmonary tuberculosis which had not responded to prolonged routine therapy and that the operation was often performed on a last-hope basis, this mortality rate seems low. Conversion of the sputum from positive to negative resulted in 179 patients (89%). This greatly exceeded the sputum conversion rate among patients treated by administration of antibiotics and simple collapse methods. Ten patients were therapeutic failures.

The early results obtained in these patients are encouraging and extrapleural pneumolysis, therefore, is considered to have a definite place in the treatment of the African with pulmonary tuberculosis. Extrapleural pneumolysis is perhaps the

simplest of the major surgical interventions used in the treatment of pulmonary tuberculosis. It is of particular value in undeveloped countries in which the facilities for resection are not readily available. It may be indicated in patients in whom resection cannot be performed, as in those with disseminated lesions or with greatly reduced respiratory capacity.

Sudeck's Atrophy and the Shoulder-Hand Syndrome. J. G. Taylor. Proc. Roy. Soc. Med. **51**:879-883 (Oct.) 1958 [London].

The author believes that Sudeck's atrophy (patchy bone atrophy [osteoporosis] after injury) and the shoulder-hand syndrome (Steinbrocker 1947) are related conditions. He discusses 10 cases of Sudeck's atrophy and 6 of the shoulder-hand syndrome. Sudeck's atrophy occurs most commonly after injury in the vicinity of the wrist or ankle joints. In this series fracture of the lower end of the radius was the usual preceding injury. There are 4 characteristic features of the conditions: loss of motor function, pain, vasomotor disturbance, and osteoporosis. After the causative injury there is usually early swelling with difficulty in finger or toe movements; there is diffuse pain in the hand and wrist (or foot and ankle) which is not relieved by immobilization; the extremity becomes hot, red, and puffy with loss of the normal fine creases in the skin; hyperesthesia or paresthesia may be present; there is increasing stiffness of hand or foot in which spasm seems to play a part. When the complication follows a Colles' fracture the symptoms may declare themselves soon after the injury or not become manifest until after the plaster is removed. Osteoporosis is obvious at about 6 weeks. The osteoporosis affects the cancellous tissue of the carpus, the lower ends of the radius and ulna and the extremities of the metacarpals and phalanges, and later their shafts. In the foot the corresponding bones are affected.

The shoulder-hand syndrome is a more extensive disability. Sometimes the disability of the hand may precede that of the shoulder, but usually for the first few weeks or months there is a painful, stiff, tender shoulder and a hyperemic swollen, painful hand with smooth taut skin and limited finger movement. Sometimes, however, the hand may be cold, purple, and sweating. Thereafter the disorder may resolve, or diffuse pain in the shoulder and arm may persist with increasing atrophic changes, stiffness, and osteoporosis of the hand, but decrease of swelling, and coldness instead of heat. The final stage is one of permanent disability, but it may resolve spontaneously. The shoulder-hand syndrome sometimes follows injury such as a tear of the rotator cuff, but it has been observed also after myocardial infarction, hemiplegia, cervical nerve root irritation, or herpes zoster.

Of the 10 cases of Sudeck's atrophy observed by the author 9 occurred in women, 8 of them after fracture of the wrist. In 4 of the 6 patients with the shoulder-hand syndrome the disorder was preceded by injury to the shoulder, in 1 by a cardiac infarct and in 1 no etiological factor was found. The treatment is the same for both conditions. Elevation was used to reduce swelling of the hand and the patients were instructed to perform such finger, hand, and shoulder movements as they could do without increasing their pain. During the stage of spontaneous pain physiotherapy and intensive active exercises aggravated the symptoms. When the pain had subsided, wax baths and active exercises became helpful in restoring movement. Sympathetic ganglion block, carried out in the severe cases, produced permanent improvement in only 1 of the patients. In the others the effect was only temporary. Cortisone therapy was tried in 3 patients; it failed in 2 patients with the shoulder-hand syndrome, but produced improvement and finally recovery in a patient with Sudeck's atrophy. The final outcome was fairly satisfactory, in that 6 of those with Sudeck's atrophy recovered in about 10 months; in 3 slight disability remained, and in 1 severe disability. Of the 6 patients with the shoulder-hand syndrome 4 made a complete recovery, 1 has slight residual stiffness, and 1 had severe shoulder and hand disability after 2 years.

Chemopallidectomy for Relief of Parkinson's Disease with Remarks on Selection of Cases for Operation and Improvements in Surgical Technique. J. M. Meredith. J. South Carolina M. A. **54**:357-363 (Oct.) 1958 [Florence].

The most hopeful approach to the neurosurgery of Parkinsonism is destructive chemical surgery of the basal ganglia, particularly of the globus pallidus or portions of the thalamus. The majority of neurosurgical clinics in this country favor either (1) chemopallidectomy by means of alcohol injection into the basal ganglia, or (2) the pallidotomy knife-cutting technique of McKinney. Ultrasound techniques that are utilized now in some of the research centers are so elaborate and time-consuming that they are not very practical and feasible for most hospitals in which Parkinsonism patients are being operated on.

With reference to the selection of patients with Parkinson's disease for chemopallidectomy, the most important contraindications are pseudobulbar symptoms, mental deterioration, vegetative signs, spontaneous hyperthermia and excessive sweating and salivation, respiratory difficulties such as uncontrollable hyperpnea, and psychiatric disorders. Physiologic signs of senility also contraindicate surgery, but chronologic aging, per se, does not. Parkinsonian patients with unilateral or bilateral symptoms and none of the foregoing contraindica-

tions are potentially good candidates for chemopallidectomy provided definite progression of the disease, failure of medical therapy, and a marked degree of involvement justify this course of action. Most patients over 60 to 62 years of age, especially those in wheel chairs or bedridden with oversalivation or other symptoms listed above, should not be operated on in the present state of knowledge and experience. Almost all writers today agree that the ideal candidate for the operation is under 60 years of age, preferably with only one side grossly involved, with poor response to medication, still ambulatory and in good general condition, but with diminished earning power.

With these restrictions in the selection of patients, and with the meticulous use of either (1) the chemopallidectomy technique using alcohol, or (2) the McKinney's subcortical pallidotomy knife cutting procedure, good results can be obtained in approximately 60 to 70% of patients with Parkinsonism chosen for operation. Statistically, therefore, there is as much if not more justification for neurosurgical treatment of Parkinsonism as there is for neurosurgical treatment of intractable pain, focal epilepsy, and other diseases which merit the attention of neurosurgeons. The general practitioners, who care for the large population of Parkinsonism patients, should now consider neurosurgical intervention as one possibility in the treatment of selected patients with moderately advanced lesions. Neurologists can consider the fact that neurosurgery has produced satisfactory relief for 3 years or longer in many patients with Parkinsonism.

Gastric Ulcer: Survey of the Rhode Island Hospital Cases in the Ten-Year Period from 1946 through 1955. J. R. Bernardo, C. H. Soderberg and A. V. Migliaccio. Surgery **44**:804-812 (Nov.) 1958 [St. Louis].

Of 519 patients with gastric ulcer who were admitted to the Rhode Island Hospital between 1946 and 1955, 142 were treated medically and 377 surgically. There were 364 male patients and 155 female patients between the ages of 10 and more than 81 years. Of the 364 male patients, 331 had benign ulcers and 33 had malignant ulcers; of the 155 female patients, 138 had benign ulcers and 17 had malignant ulcers. Duration of symptoms in the entire group of 519 patients averaged 4.7 years, as compared with an average duration of 1.3 years in the group with malignant ulcers. There was no difference in significant weight loss between the patients with benign and malignant ulcers. The incidence of massive hemorrhage was higher (11%) among the patients with benign ulcer than that (4%) among the patients with malignant ulcer. The presence of a duodenal ulcer does not rule out malignancy in an associated gastric ulcer, since 3 (6%) of the 50 patients with malignant ulcer had an associated duodenal ulcer. Multiple gastric ulcers were associated only with benign lesions.

Of the 469 patients with benign ulcer, 179 were tested for free acid and 25 (14%) of these showed absence of free acid; thus a significant number of patients with benign gastric ulcer had achlorhydria. Of the 30 patients with malignant ulcer who underwent this test, 12 (24%), however, had elevated acid values of 41 and more units. Therefore, the determination of free acid cannot be considered a reliable diagnostic tool. Gastroscopy has been unreliable in the authors' experience. Gastrointestinal roentgenographic examinations were performed on 301 of the 519 patients. Of 151 patients whose ulcer was considered benign roentgenographically 10 had malignant ulcers, the accuracy of the diagnosis being 93.8%. Of 36 patients with a roentgen diagnosis of malignant ulcer, a pathological diagnosis of malignant ulcer was made in 11 (23.4%). The overall x-ray accuracy on both benign and malignant lesions was 78%, which is only slightly lower than the 85 to 90% reported by other workers. With increasing size of a gastric ulcer the chance of its being malignant, increases as a rule, but the 5 largest ulcers, all over 6 cm. in diameter, were benign. Thus the size of the ulcer, although it is of some help in determining the presence of malignancy, cannot be taken as a reliable guide to the differential diagnosis of the individual lesion. Benign ulcers are more common in all areas of the stomach compared with the malignant ones. About 1 out of 5 lesions of the antrum, excluding the prepyloric area, was maligant. One out of 7 ulcers in the prepyloric area proved to be malignant.

Of the 142 patients treated medically, 17 (12%) died, including 12 dying from hemorrhage so severe as to prevent their being brought into condition for surgical treatment. Of the 377 patients treated surgically, 25 (6.6%) died. Subtotal gastrectomy was performed electively for gastric ulcer on 318 of the 377 patients; a high rate of minor complications (30%) and an operative mortality rate of 4.1% was noted.

Intervertebral Disc Removal and Spine Fusion. E. L. Compere, W. Schnute, C. L. Compere and R. G. Thompson. Am. J. Surg. **96**:624-630 (Nov.) 1958 [New York].

Of 154 patients with herniated intervertebral disk lesions who were operated on by the authors between 1945 and 1952 and were subjected to spine fusions combined with surgical removal of the disk, 120 answered a questionnaire which was sent to them in an attempt to evaluate the end-results. Of these 120 patients who had been followed for periods of from 4 to 11 years, 83 were between the ages of 31 and 50 years, 17 were less than 30 years of age and 20 were between the ages

of 50 and 70 years. Fifty-three patients (44.1%) had obtained excellent results, 32 (26.6%) good results, 21 (17.5%) satisfactory results, and 14 (11.8%) poor results. Only 21 (17%) of the 120 patients complained of residual back pain. Adding spine stabilization procedures to simple disk excision did not cause any increased incidence of morbidity in this series of patients as compared with those undergoing only a simple disk excision. The average duration of the patient's stay in the hospital was 18.4 days, which was not much longer than that of patients on whom only the simple procedure was performed. The results obtained were far from perfect but with increased attention to the finer details of spine fusion technique they can be improved. Although some of the patients exhibited a pseudarthrosis, these spines were remarkably stable due to dense fibrous tissue formation resulting in a decrease in back pain.

Surgeons who evaluate end results on a basis of relief of sciatica alone tend to ignore a major disability factor. Backache is the cause of more chronic disability than nerve pain from sciatica. No end-result study can be accepted unless it is based on an evaluation at least 4 to 5 years after surgical intervention. The reported data suggest that a spine fusion procedure should be performed on all patients from whom a ruptured or herniated intervertebral disk is removed. Most patients with simple disk excision will undergo subsequent degenerative changes in the facet joints of the lumbar spine. Patients who have had a disk removed and later require a fusion dread the second operation much more than the first, and all degrees of anxiety and psychoneurosis may be seen in these patients. The authors have been unable to arrive at any reliable criteria for differentiating among those patients who will not need spine stabilization and those in whom back pain will be so incapacitating that a second operation for spine stabilization should be performed. Pantopaque, although believed to be rapidly absorbed in the subarachnoid space, was observed to be present in significant amounts as long as 10 years after myelography. However, no significant reactions were noted to the prolonged presence of the Pantopaque mediums.

Sarcoidosis of the Small Intestine (Its Relation to Crohn's Regional Ileitis). M. Janbon and L. Bertrand. Presse méd. **66**:1491-1494 (Oct. 1) 1958 (In French) [Paris].

The authors report on a 30-year-old woman in whom a progressive obstruction of the small intestine developed while she was subjected to a combined antituberculous treatment for acute miliary tuberculosis of the lungs. Mycobacterium bacilli were absent in the sputum, in the gastric juice, and in the feces; repeated tuberculin tests were negative. Roentgenograms of the gastrointestinal tract made during the subacute phase of bowel obstruction showed delayed passage and considerable dilatation alternating with narrowing of the jejunoileal loops. Roentgenograms of the chest did not show any pulmonary lesion which was seen two months previously, thus the antituberculous treatment seemed to have completely and spontaneously cured the acute miliary tuberculosis of the lungs. Laparotomy revealed more or less stenosed, fleshy thickening at various parts of the intestinal wall, more marked in the terminal ileum and extending to the jejunum. There was no ulceration of the mucous membrane and no enlargement of the mesenteric lymph nodes. The operative specimen, which consisted of 15 cm. of the most stenosed segment of the terminal ileum, disclosed numerous sarcoid tubercules with a few giant cells, but there were no signs of necrosis. Confluent masses of sarcoid lesions were more frequent in the submucosal areas, but involvement of the muscular coat and of the subperitoneal coat were also seen.

The administration of cortisone was started 15 days after the operation in doses of 50 mg. daily for one month. The patient's postoperative improvement was slow and was probably aided by cortisone therapy. Her clinical cure has now been maintained for four years, and she leads a normal life. The authors do not share the opinion concerning correlation between tuberculosis and sarcoidosis, and believe that the rare condtion of sarcoidosis of the ileum should be differentiated from Crohn's regional ileitis as well as from tuberculosis.

Multiple Cancers in Colon Surgery: Report of 162 Cases. R. A. McGregor and H. E. Bacon. Surgery **44**:828-833 (Nov.) 1958 [St. Louis].

Of 1,788 patients with microscopically verified cancer of the colon and the rectum who were admitted to the department of proctology of Temple University Medical Center between September, 1940, and May, 1958, 162 (9.1%) had multiple primary malignancies. There were 90 men and 72 women. Ninety-four of these 162 patients had multiple primary lesions of the large intestine alone, an incidence of 58.1% among the patients with multiple primary malignancy and an incidence of 5.3% among the total number of patients with cancer of the colon and rectum. The remaining 68 patients (41.9%) had involvement of large intestine and of organs or systems other than the colon. Of the 94 patients with multiple primary lesions of the large intestine alone, 60 were men and 34 were women. In addition to these 60 men, there were 9 men with second or third primary cancers in the upper gastrointestinal tract. Only 1 woman in the entire series had a second carcinoma involving the upper gastrointestinal tract. These data suggest that men show a definite predisposition to involvement of

the gastrointestinal tract. Twenty-nine (40%) of the total number of 72 female patients had cancer of the large intestine and in addition primary malignant neoplasia of the sex organs and breast.

It is evident that multiple primary malignancy, of the large intestine at least, is not a rare or even an unusual phenomenon. Any patient with a carcinoma of the rectum or the colon has an increased risk of cancer occurring at other sites, simultaneously or at different time intervals. The relative incidence of primary multiple cancer may be high or low according to the various reports by other workers, but the fact that it is a definite possibility is the important point. All physicians must be alert to this possibility and must abide by the following rules when a cancer patient is dealt with: 1. Preoperative investigations should include a careful physical examination, proctosigmoidoscopy, and roentgenologic examinations. In men, upper gastrointestinal roentgenograms are advisable. The slightest gastrointestinal symptom in women should warrant barium meal studies. 2. During surgical intervention meticulous exploration of the colon and of all abdominal organs should be performed. Coloscopy often reveals lesions missed by palpation. 3. After the operation patients should be checked at regular intervals, both clinically and roentgenographically. Each patient should remain on the cancer detection list because of the possibility that an additional primary cancer may occur even though the patient's survival time, whether it be 5, 10, or even 20 years, suggests theoretically a surgical cure.

Significance of Peroperative Cholangiography in the Management of Gallbladder Disease. P. A. Ykelenstam. A. M. A. Arch. Surg. **77**:684-688 (Nov.) 1958 [Chicago].

The author reports on 20 men and 80 women, between the ages of 27 and 88 years, with gallbladder disease, who were operated on at the St. Canisius Hospital in Nijmegen, The Netherlands, and on whom cholangiography was routinely performed in the course of cholecystectomy. A comparison was made with a series of 100 patients in whom the gallbladder was removed without the aid of cholangiography in the course of the surgical intervention. Conventional indications for exploratory examination of the biliary system were present in 64 of the 100 patients operated on with the aid of cholangiography. Shadows were revealed by the cholangiography in 19 patients, and in 3 of them the shadows were suspected to be ascribable to air bubbles. Occlusion of the papilla of Vater appeared on roentgenographic evidence to be present in 10 patients and was confirmed by exploration in 8; in 16 patients the duodenum did not fill with contrast medium after a single injection; after a second injection no filling was observed in 12 patients. In 8 patients this appeared to be due to the presence of a calculus in the papilla. In the remaining 4 patients no pathological changes or calculi were found. In 15 of 37 patients with a history of jaundice, roentgenograms of the opacified area revealed shadows (probably caused by calculi); in the course of the ensuing choledochotomy stones were actually found.

The reported data suggest that unnecessary exploration of the bile ducts was prevented in 40 patients, so that drainage of the common bile duct could be avoided and, consequently, the risk of complications reduced and the time of hospitalization shortened. In 4 patients exploration did not yield any results, and in 3 of them the presence of air bubbles had been suspected previously. In 5 patients in whom no indications for choldochotomy appeared to be present, the cholangiogram revealed shadows caused by stones and, on exploration, stones were found. This experience alone would seem to be sufficient justification for the routine performance of contrast roentgenography during cholecystectomy. There were indications for exploration of the common bile duct in 56 of the 100 patients in the control series. Exploration was performed in 50 of the 56 patients, and in 23 of the 50 patients exploration proved to be unnecessary. The use of cholangiography in the course of surgical intervention is recommended in all operations performed on the basis of suspected gallstones or biliary obstruction, hypersensitivity to iodine or the patient's precarious condition being among the only reasons for abandoning this type of examination. With adequate technique and sufficient experience, cholangiography performed in the course of surgical intervention is considered a reliable diagnostic aid in establishing the presence of calculi in the bile ducts.

Metastasized Malignant Thymoma and Myasthenia Gravis. M. R. Poinsi, J. Chapin, H. Payan and G. Darcourt. Presse méd. **66**:1506-1508 (Oct. 1) 1958 (In French) [Paris].

Malignant thymoma metastasizing to the liver was found to be the cause of death in a 24-year-old woman. Severe asthenia and loss of weight which had existed for three years had been attributed to over-exertion. Fluoroscopic examination revealed a shadow of doubtful significance in the middle mediastinum. The patient's condition gradually grew worse during the next two years; severe muscular disorders appeared, and she had difficulty in swallowing, in chewing, and in talking. Neurological examination revealed myasthenia gravis which was typical except for the fact that it could not be brought under control by the administration of prostigmin. Roentgenograms of the thorax made from the anteroposterior and lateral plane showed

enlargement of the thymus. On abdominal palpation the outlines of the liver were found to be irregular and bosselated. Laparoscopy revealed a typical secondary neoplasia. The operative intervention undertaken for the purpose of removing the thymic tumor disclosed a large (10 cm. in vertical diameter, and 7 cm. in horizontal diameter) lobulated and woody thymus, which was inoperable, extending to the middle portion of the mediastinum on the right side. There was extensive metastasis to the liver, characterized by multiple nodules (varying in size from a hazelnut to that of an apricot) on the left lobe of the liver, and by a tumor involving almost completely the right lobe of the liver. There was no direct continuity between the liver and the thymic tumor.

A transient improvement was noted in the patient's condition after the exploratory thoracotomy, and for the period of two months the ingestion of from 7 to 8 tablets daily of prostigmin was sufficient to alleviate the symptoms. Her liver, however, gradually increased in size, severe motor disturbances involved the arms, and difficulty in breathing developed despite the administration of 27 tablets daily of prostigmin. The patient died of asphyxia five months after the operation. Histologic study of biopsy specimens taken from the liver and the thymic tumor revealed a mature thymic epithelioma of complex structure containing epithelial elements of different morphologic modifications, and small lymphocyte or thymocyte cells.

A review of the literature shows that malignant tumors of the thymus in patients with myasthenia gravis are unusual, but the occurrence of metastasis to the liver is still more exceptional.

GYNECOLOGY & OBSTETRICS

Pathology and Treatment of Mammary-Duct Fistula. D. H. Patey and A. C. Thackray. Lancet **2:** 871-873 (Oct. 25) 1958 [London].

The authors report on 7 women, between the ages of 24 and 48 years, with a fistula of a large mammary duct near the nipple who were operated on at the Middlesex Hospital in London. The youngest patient had had no children and the oldest had had 2. The condition was associated with some degree of retraction of the nipple in 6 of the 7 patients. The typical history was that of the occurrence of a lump eccentrically situated under the areola, sometimes but not always with the clinical features of an abscess. The abscess either ruptured or was opened and drained, but did not permanently heal. Periods of apparent healing alternated with periods of discharge from a small granulating orifice situated at the margin of the areola. The fistulas were excised completely up to the opening of the involved duct at the nipple. The operative specimens were studied pathologically. Microscopic examination revealed that the condition is associated with a duct lined with squamous epithelium, in contradistinction to the normal lactiferous ducts which are lined by 2 layers of cells, the inner columnar epithelium and the outer flattened myoephithelium. In 2 specimens, the presence of sebaceous glands opening into the abnormal duct pointed to a congenital abnormality. In others, the abnormal lining of the duct may result from squamous metaplasia; there is, however, evidence against this view and all cases may represent a congenital abnormality.

Mammary-duct fistula is a common cause of persistent or recurrent inflammation and discharge after a periareolar abscess. The rational radical treatment is complete excision of the fistula and the abnormal duct; if exteriorization proves in practice to be equally satisfactory, it may be preferable as interfering less with the normal ducts of the nipple.

Cancer of the Breast: A Study of Short Survival in Early Cases and of Long Survival in Advanced Cases. D. W. Smithers. Am. J. Roentgenol. **80:**740-758 (Nov.) 1958 [Springfield, Ill.].

The author reports on 2,648 patients with cancer of the breast seen at the Royal Marsden Hospital in London, England, between the years 1937 and 1953. In 583 (22.0%) of these patients the tumor was in stage I and 38 (7.0%) of these died within 2 years of treatment. At the time of death they had distant blood-borne metastases with a predominance of those in the liver and the brain. The grade of tumor had been recorded in 19 of the 38 patients. Three of those had grade I tumors, 8 had grade II and 8 other patients had grade III tumors. Eleven patients had tumors of the inner half of the breast. Treatment by surgery and irradiation gives excellent results as long as the disease is still well localized, but these methods fail if blood-stream dissemination has occurred. The factors of chief importance in judging direction of spread and in estimating the chance of dissemination in clinically early cases are the grade and size of the tumor, the length of history, the site of the tumor, and the age of the patient. Standard treatment applied rigidly according to the stage alone represents a denial of clinical judgment. Unfavorable prognosis should limit the use of surgical methods, which may make matters worse if a complete success is not warranted. Large medial tumors in stage I with a short history are, however, the only ones in which irradiation before mastectomy is often indicated especially when the patient is obese and difficult to examine. The prognosis is comparatively bad for patients with tumors in the early stages located in the inner half of the breast in contrast to those in the outer half of the breast. This is due to the fact that tumors of the inner half of the breast lead to

more frequent involvement of the clinically less easily detectable parasternal lymph nodes. Thus patients with tumors of the inner half of the breast in an early stage require special care in treatment, and the question of preference for surgery or irradiation in the less malignant grades is still undecided. Older women tend to wait longer before coming for treatment and have therefore a more unfavorable stage distribution than younger women, but age also affects the prognosis in the young in as much as hormonal influences are concerned. Tumors developing during pregnancy or lactation have a relatively bad prognosis whereas those developing shortly before the menopause may have a relatively good one. In all young women before the menopause who have grade III tumors, multicentric origin, extensive perivascular or perineural lymphatic permeation or involvement of axillary fat, an artificial menopause should be considered as part of the first planned treatment.

Another study in 293 patients with cancer of the breast, stage IV, admitted to the same hospital between 1940 to 1949 showed that 2 patients survived 3 years or more; 9 of these were premenopausal and 12 postmenopausal by more than 10 years. There were no 3 year survivors among the patients in stage IV who were treated within 10 years after the menopause. In 7 of the 9 patients in the premenopausal group, menopause was induced and initial roentgenotherapy was given. Three of the 7 patients were still alive 13, 10 and 9 years afterwards (2 with no further treatment other than the initial roentgenotherapy and induced menopause; 1 at 10 years after the whole therapeutic gamut of oophorectomy, adrenalectomy, testosterone injections, and further irradiation). The remaining 2 of the 9 patients were treated with estrogens at the time of their initial roentgenotherapy. Eight of the 12 postmenopausal patients who survived 3 years or more were given estrogens, all had roentgenotherapy and 1 had in addition local mastectomy.

These data show that although early breast cancer is regularly curable, some patients may nevertheless die within a short time in the course of the treatment. The invasiveness and danger to life once advanced breast cancer has reached this stage cannot well be denied, but estrogen treatment combined with irradiation may give some long-term survivals.

The Histogenesis of Ovarian Tumours. R. E. Rewell. J. Obst. & Gynaec. Brit. Emp. **65**:718-726 (Oct.) 1958 [London].

The author reviews observations on several hundred ovarian tumors seen chiefly in one center in England and in one in India. A table lists the diagnoses in 209 patients at the Women's Hospital, Liverpool, England, and in 118 patients at the Government Hospital for Women and Children, Madras, India. The author saw relatively more rare tumors than are listed in the table, because specimens of doubtful and interesting tumors were often sent to him from other institutions, so that he estimates that he studied approximately 500 ovarian tumors. He found that adenocarcinoma was relatively more frequent in India than in England, there being 37 adenocarcinomas among 118 ovarian tumors studied in Madras and only 34 among 209 in Liverpool.

He found that the boundaries between many of the accepted types of ovarian tumors are much less clear than is usually realized, e. g., the granulosa-cell and thecal-cell tumor form a continuous series, nor can some Brenner tumors be divided from them sharply, while these again merge into some types of pseudomucinous cystadenoma. These tumors form a group by themselves, what may be termed the "stroma-follicle" group and they are best regarded as derived from the common stem of theca and follicle cells in the normal adult ovary at quite a late stage in their differentiation. Among these tumors structural differentiation by no means runs parallel with functional differentiation and vice versa. The series confirmed previous observations that the appearance of the Brenner tumor, and possibly that of the pseudomucinous cystadenoma, is nonspecific and may be produced by different modes of development, nor are these in themselves of a uniform pattern. The terms "granulosa-cell," "thecal-cell," and "Brenner" applied to tumors are of clinical convenience only. These terms must not be thought of as excluding a common origin for the group, while many individual tumors fall into areas of overlap between them even when used in a purely descriptive sense.

Teratomas are probably derived from a distinct stem of primitive cells, as also are dysgerminomas and probably arrhenoblastomas. Routine study of ovaries removed at operation confirms modern theories of the close relationship of stromal and follicle cells and tends to support the possibility of the origin of new follicles in the adult ovary.

Fetal Electrocardiography, with Special Reference to Early Pregnancy. S. D. Larks and K. Dasgupta. Am. Heart J. **56**:701-714 (Nov.) 1958 [St. Louis].

The authors recorded 260 fetal electrocardiograms which were obtained from 145 pregnant women. In certain of these women as many as 16 consecutive recordings were obtained through the full gestational period. Between the 16th and 22nd weeks of pregnancy the fetal electrocardiograms became large, sharp, and clear. At this time and afterward the fetal electrocardiogram may become of diagnostic importance. The earliest fetal complexes were recorded in this series, at 11½ to 15 weeks; they were directed downward. Judging by the consistent relationship which was observed between such complexes and breech presentations at

later stages of gestation when clinical or roentgenographic evidence was available, it would seem that, ordinarily, the fetus presents by the breech at this early period of pregnancy. Similarly, the fact that the fetal-QRS changed to an upright complex in the usual case at about 20 weeks suggested that rotation to the more common vertex presentation takes place at about this time. It is possible that a combination of rotation about 2 axes, not only the transverse but also the longitudinal axis of the fetus, might make changes in the fetal electrocardiogram which could resemble breech-to-vertex rotation. The fetal electrocardiogram thus provides rapid information as to the presence of a living fetus, and its presentation.

Recordings from 4 sets of twins are presented which indicate the value of fetal electrocardiography in cases of multiple pregnancy. A diagnosis of multiple pregnancy was made at 21 weeks in a pregnant woman from whom tracings were obtained as follows: the first at 16 weeks, and the second, third, and fourth tracings at 21 weeks. This electrocardiographic diagnosis was immediately confirmed roentgenographically. Actually, it is possible to make the diagnosis from the tracing of the 16th week. In other cases, recordings of the fetal electrocardiogram in utero, and subsequent electrocardiograms of the newborn infant were obtained for both vertex and breech presentations. The identity of the complexes was beyond doubt. The presence of a cardiac anomaly in the fetus was revealed in another case at the 20th week of gestation by several unusual features in the electrocardiographic tracing. The direction of the complex seemed to indicate a vertex presentation, yet roentgenographic evidence showed a breech. The complexes were unusually wide and notched, suggesting conduction difficulties. The complexes showed the prolonged overshooting which cardiologists usually refer to as S-T segment displacement. In this case the infant showed delayed respiration at delivery and survived only 5 days. At autopsy, coarctation of the aorta was observed. Utilizing presently available instruments and techniques fetal electrocardiograms thus can be recorded in utero even early in pregnancy and may be a valuable diagnostic aid in obstetrics and allied fields. In general, fetal electrocardiography provides positive results from 2 to 6 weeks before the first auscultation of the fetal heart tones.

Recurrent Pregnancy Toxaemia. D. W. S. Gordon and M. R. Fell. J. Obst. & Gynaec. Brit. Emp. **65:** 727-733 (Oct.) 1958 [London].

That toxemia of pregnancy does tend to recur has been known for many years, but little work has been done on this problem, and so it was decided to assess, as accurately as possible, exactly what is the chance of pre-eclamptic toxemia recurring. The theory that a renal lesion was the factor behind the recurrence has now been discarded. However, the possibility that these women were getting toxemia again because of an inherent tendency to develop essential hypertension has gained some support and, as a corollary to the main problem, it was decided to see if there was any evidence to substantiate this theory. Finally, an analysis was made of 3 factors which it seemed might influence the chance of recurrence—namely, the severity of the initial toxemia, its duration, and time of onset in pregnancy. The 996 cases of toxemia which occurred at a maternity hospital during a period of 5 years, when 17,562 deliveries were made, form the basis of this report. The criterion for toxemia was a blood pressure of 140/90 or over, together with the presence of albuminuria and/or definite edema. The combination of hypertension and edema without albuminuria was very unusual.

In commenting on their findings the authors state that the chance of any woman who has had pre-eclamptic toxemia developing it again in her next pregnancy is 45%. If pre-eclamptic toxemia occurs in 2 consecutive pregnancies the risk of a further recurrence rises to 72%. Should it occur 3 times running, then toxemia a fourth time is almost a certainty. If a woman who has had pre-eclamptic toxemia does not develop it again in her next pregnancy then the risk of her ever developing it again in subsequent pregnancies is only 6%. Pre-eclamptic toxemia developing in association with multiple pregnancy behaves differently and merits consideration as a separate problem. Thus there were 10 women with twins, in all of whom signs of pre-eclamptic toxemia developed for the first time during the twin pregnancy, but it developed in none of these women during the subsequent pregnancy. It may be that toxemia associated with multiple pregnancy does not carry the same risk of recurrence in future pregnancies as does toxemia occurring with a single pregnancy.

Patients classified as having a severe form of pre-eclamptic toxemia appeared to have a higher chance of recurrence. However, it cannot be claimed that severity itself is the deciding cause. Eclampsia carries less risk of recurrence than toxemia without fits. The length of time the toxemic process is active may have some bearing on this point, if, as is often the case, eclamptic fits supervene on a fulminating type of pre-eclamptic toxemia, so that although this is toxemia in its most severe form, the whole process is relatively short-lived. In this connection it is pointed out that with the present-day trend toward early induction of labor, the duration of the process in relation to recurrence is of doubtful significance. No evidence was found on analyzing subsequent blood pressure levels to suggest that these women were developing recurrent toxemia because of the associated onset of essential hypertension. The time of onset of the

toxemic process is of doubtful significance especially as a higher proportion of the "severe" cases occurred in the earlier onset group. This survey was conducted by a retrospective investigation and has all the disadvantages associated with this. There are many other factors that could be investigated.

The Determination of the Genetic Sex. G. Sansone and A. Tomassetti Levi. Minerva pediat. **10**:925-932 (Sept. 22) 1958 (In Italian) [Turin, Italy].

The genetic sex according to the leukocyte morphology test devised by Davidson-Smith was investigated in 3 groups of persons. The test conducted by each author independently from each other indicated the correct genetic sex in one group of 300 children and adults with normal sexual features. The sex identity was not disclosed to the investigators until after the diagnosis was made. The number of drumsticks was larger in the younger than in the older individuals.

The second group consisted of 67 newborn infants, 36 being premature and 31 born at term. The percentage of drumsticks in the immature female newborn infants was on average 8.3% with variation from 3 to 15%. The percentage of drumsticks in mature female newborns was on average 7.5% with variation from 2.8% to 16%. Ten pairs of female dichorial and enzygotic twins were included in this group. The small number of newborn infants in this group did not permit one to draw any conclusion. The third group consisted of 16 persons, aged between 1 month and 21 years, with gonadal dysgenesis, 14 of whom had the Bonnevie-Ullrich syndrome and 2 had the ovarian agenesis. The test was repeated several times. Sex chromatin test was negative (male) in 10 of these patients and positive (female) in 4. Examination of the smears from the oral mucosa suggested a chromatin-negative response in 1 patient in whom the response to Davidson-Smith test was equivocal. The sex chromatin test in 2 patients with ovarian agenesis suggested masculine genetic sex. The determination of the genetic sex by Davidson-Smith technique in the third group was significant, because most of the patients passed the puberal age and did not show any secondary sexual features nor had they menstruated.

PEDIATRICS

Pancreatitis in Young Children. J. Collins. Arch. Dis. Childhood **33**:432-436 (Oct.) 1958 [London].

Pancreatitis is rare in young children. The author describes the pathologic changes found in the pancreas at autopsy in 4 children, all aged 2 years or less. Three of the children concerned were Bantu of N. Rhodesia and were the only ones found to have pancreatitis in the routine examination of material from 100 consecutive autopsies on African children. The fourth child, included for comparison, was an Edinburgh girl and the only case of pancreatitis in the records of 1,812 consecutive postmortem examinations. In each of these children inspissated secretions had caused the dilatation, obstruction, and subsequent rupture of intralobular ducts, and in two cases the resulting pancreatitis had been confined to a very small area and was undergoing healing by fibrosis. It is suggested that this inspissation is brought about by a combination of vagal stimulation, dehydration, and the absence of normal pancreatic secretions over a period of time probably measured in days. If this theory of the cause of these intraductal obstructions is correct then, apart from the normal procedures to remedy dehydration, other measures to overcome vagal stimulation (where this is present) and to encourage normal pancreatic secretions are indicated in all very young sick children.

A Test for Coeliac Disease. W. W. Payne and V. Jenkinson. Arch. Dis. Childhood **33**:413-416 (Oct.) 1958 [London].

The relationship between wheat flour in the diet and the development of symptoms in children with celiac disease observed by Dicke in 1950 has been established. Subsequent investigations indicated that the injurious factor occurs principally in the gliadin fraction. Weijers and van de Kamer in 1955 used gliadin for testing, hoping that the test would be helpful in the diagnosis of celiac disease. In order to determine the value of this gliadin tolerance test, the authors performed it on a series of children with celiac disease and on controls. Thirty-three patients with celiac disease were studied. The diagnosis was made according to stated criteria in 25, and in 8 it was based on clinical data associated with the response to a gluten-free diet, and relevant biochemical investigations were not made. Two of the children were in the active phase of the disease in that treatment had not been instituted when they were tested. Eight children had been on a gluten-free diet for periods of a few days to one month before their gliadin tolerance test. These children have since shown a satisfactory response to the therapeutic diet. The rest of the patients had been treated for some years, having had periods on a gluten-free diet and on a normal diet. Some children, who had been treated for more than 4 years, still deteriorated when returned to a normal diet. A few patients had apparently recovered after prolonged treatment; they had shown no recurrence of symptoms when returned to a normal diet and growth continued at the expected rate. Six children in this series were either undiagnosed or untreated for a long time after the onset of symptoms.

Contratest cases were selected from convalescent patients who had had diseases with no alimentary tract involvement, with the exception of one child, who was a normal healthy unlike twin of one of the patients with celiac disease. Four children who were convalescent from disorders of the alimentary tract from causes other than celiac disease formed a second contratest group. Gliadin was prepared according to the procedure recommended by van de Kamer. The authors found that the increase of apparent plasma glutamine after a test dose of gliadin was significantly greater in children with celiac disease than in contratest children. Children convalescent from gastrointestinal dysfunction from causes other than celiac disease showed an increase intermediate between healthy children and those with celiac disease. There was no quantitative relation between increase of plasma glutamine and phase of the disease, whether acute or nonsymptomatic through withdrawal of wheat and rye gluten from the diet. Diet appeared to have no influence on the degree of increase of plasma glutamine. The overlap of range of results from contratest subjects and celiac disease patients is considerable and does not recommend the test as a diagnostic one.

OTOLARYNGOLOGY

Cytologic Diagnosis in Otorrhinolaryngologic Neoplasms. T. Ferreira Lorenzi. Rev. Hosp. clin. **13:** 291-296 (July-Aug.) 1958 (In Portuguese) [São Paulo].

The cytologic diagnosis of otorrhinolaryngologic cancer is based on the aspect of the tumor cells and the character of the structures which form the cells. The cells are atypical. They are arranged in abnormal groups. The nuclei present abnormalities of size, number, limits, contents of chromatin, mitoses, and nucleoli. As a rule the nuclei are much larger than those of normal cells. The cytoplasm is scanty and the nucleus-cytoplasm ratio is increased. Seventy patients with malignant otorrhinolaryngologic tumors were observed at the Clinica Otorrinolaringologica of the Hospital das Clinicas of the University of São Paulo. Cancer was located in the nose (13 cases), the maxilla (9), the mouth (22), the nasopharynx (4), the larynx (9), the neck (9), and other otorrhinolaryngologic structures (4). A cytologic diagnosis was made by the Papanicolaou and Leishman's methods of stained smears. The smears were prepared with material obtained by scraping of the tumor, puncture, surgical biopsy and scraping of surgical specimens. The cytologic diagnosis was positive for cancer in 66 out of 70 patients. There were 3 false positive results in the smears prepared with material from the mouth of a patient with Southamerican blastomycosis, the larynx of a patient with laryngeal tuberculous ulceration and from the material obtained by puncture of an enlarged cervical lymph node in a patient with scrofula. The only false negative result was on a smear prepared with material from a mixed tumor of the parotid gland with carcinomatous degeneration. The author concludes that the cytologic diagnosis by the Papanicolaou and Leishman's methods is of value in the diagnosis of cancer of the mouth, pharynx, larynx, and other otolaryngologic structures. It is indicated in patients with clinical symptoms of otorrhinolaryngeal cancer when the results of histologic examination are negative. It is also of value in a differential diagnosis between oropharyngeal carcinoma and blastomycosis.

THERAPEUTICS

The Use of Raubasine in the Treatment of Angina Pectoris and of Cerebral Atherosclerosis. J. Pieri, M. Wahl, and J. Casalonga. Presse méd. **66:**1523-1525 (Oct. 4) 1958 (In French) [Paris].

Raubasine, one of the alkaloids from Rauwolfia serpentina, is a pure sympatholytic agent capable of reversing the action of adrenalin and noradrenalin. It is essentially an arterial vasodilator with a gradual and persistent spasmolytic action. Lessening in both severity and frequency of anginal crises was pronounced in ⅓ and light in ½ of a group of 50 patients with angina pectoris who were treated with raubasine. Three mg. per day for 6 to 8 weeks benefited both patients with functional angina and those with confirmed coronary disease. Small doses bring a therapeutic improvement which probably lasts over a longer period of time than larger doses would produce. In 23 cases of confirmed ischemia of the myocardium, 7 were greatly improved, as much functionally as electrocardiographically, and 6 showed clinical improvement of the myocardium. Most of these patients had particularly tenacious and severe myocardial disorders of early appearance. Electrocardiographic improvement was in the modifications that seemed to be related to arterial spasm. Long duration of anginal disease is not a contraindication of raubasine. Raubasine associated with the total alkaloids of rauwolfia and with cardiac stimulants was given to patients with tachycardia and hypertension to treat the first symptoms of overloading of the myocardium. The advantages sought were (1) a neurosedative and bradycardiac action to complete the effect of mild cardiac stimulants, (2) a direct influence by raubasine on the circulation in the heart muscle, and (3) a diminution of the doses of total hypotensor alklaloids through the reinforcement exerted by raubasine. Of 22 patients with tachycardia and hypertension who were treated, only one developed symptoms of asystole.

Raubasine was used to treat the sequelae of various cerebrovascular attacks, the quality of results being in proportion to the precocity of treatment. Treatment with 3 to 5 mg. of raubasine coincided with disappearance of paresis of central origin or of motor awkwardness which were not accompanied by the Babinski sign in a little more than one half of the patients recently afflicted with clinical symptoms of cerebral ischemia. Treatment with raubasine is also effective in patients whose symptoms are more functional than organic, and are of long duration. Difficulties of equilibrium, vertigo, and persistent headache either disappeared or were strongly attenuated after doses of 3 mg. of raubasine for 1½ months in one third of 22 elderly patients with hemiplegia who were afflicted with various manifestations of atherosclerosis. Raubasine exerts a curative and possibly preventive action upon ischemic apoplectic attacks. It seems to gradually improve the circulation of blood in the myocardium and its results are not definite before 6 to 8 weeks of treatment. In this study it was well tolerated, had no side-effects, and provided encouraging results considering the usual severity of the conditions treated.

Fecal Enema as an Adjunct in the Treatment of Pseudomembranous Enterocolitis. B. Eiseman, W. Silen, G. S. Bascom and A. J. Kauvar. Surgery 44:854-859 (Nov.) 1958 [St. Louis].

The authors report on 3 men, between the ages of 46 and 68 years, and 1 45-year-old woman with pseudomembranous enterocolitis to whom retention enemas composed of normal feces suspended in sodium chloride solution were administered in an attempt to re-establish the normal intestinal bacterial flora. Cultures of the stool of all 4 patients had revealed Staphylococcus pyogenes var. aureus before this therapy was instituted. The latter is based on the fact that staphylococcic overgrowth occurs when other organisms disappear and that reintroduction of the bacteria, viruses, and bacteriophage normally found in the colon might re-establish the balance of flora with subsidence of staphylococcic predominance and the distressing symptoms caused thereby. In each of the patients, the clinical course was markedly improved and the Staphylococcus pyogenes var. aureus which grew in pure culture before the treatment disappeared from the stools and was replaced with normal colonic nonpathogenic agents after this therapy.

Attempts to produce in 2 dogs a progressive enteritis or bloody diarrhea within a previously sterilized isolated intestinal segment by the instillation of a pure broth culture of tetracycline-resistant Staphylococcus pyogenes var. aureus daily for 4 days failed. Thus it has not been possible to evaluate the fecal enema under controlled conditions. It is suggested that this simple yet rational therapeutic method should be given more extensive clinical evaluation.

PATHOLOGY

Splenoportal Occlusion in Patients Without Enlarged Spleen. G. Sotgiu, C. Cacciari, and E. Pisi. Minerva med. 49:3247-3251 (Aug. 29) 1958 (In Italian) [Turin, Italy].

The authors report on 60 patients with occlusion of the splenoportal veins, 52 of whom had enlarged spleen. Splenoportal occlusion associated with the enlarged spleen was present in 6 patients with a nonneoplastic disease and in 6 patients with a neoplastic disease of either the pancreas, biliary duct, or stomach. Of 8 patients without enlarged spleen, 6 had neoplasm, 1 had portal thrombosis accompanying calculous cholangitis, and 1 had splenic thrombosis accompanying cirrhosis. The authors suggest that the occlusion of the splenic vein is associated with an enlarged spleen mostly in those instances where the spleen is affected by an inflammatory or an infective process, such as in thrombophlebitic disorders. Splenoportal occlusions apparently do not cause the enlargement of a normal spleen, that is one which is not directly involved in a pathological process. The preceding 6 patients without enlarged spleen and a neoplastic disease of another organ illustrate this point. In the opinion of the authors the spleen did not enlarge in these patients because it remained intact. It is possible that a diminished arterial flow adjusted itself gradually to a diminished venous flow and thus did not produce the enlargement of the spleen.

The Experimental Production of Atherosclerosis in Swine Following the Feeding of Butter and Margarine. H. C. Rowsell, H. G. Downie and J. F. Mustard. Canad. M. A. J. 79:647-654 (Oct. 15) 1958 [Toronto].

The authors studied the changes in blood lipids and blood coagulation and the development of atherosclerosis in 33 swine, divided into 3 groups, fed either a low-fat diet or isocaloric diets rich in butter or margarine. Some atherosclerosis was observed in swine on a low-fat diet. The high-fat diet containing margarine as the fat source caused little increase in the amount of atherosclerosis, while a high-fat diet containing butter produced a considerable increase in the amount of atherosclerosis. There was no increase in blood cholesterol and phospholipid levels in the swine on the butter or margarine diets. The coagulation indexes studied at the completion of the experiment were most active in the butter-fed swine with the most con-

siderable atherosclerosis. The course of the disease and the gross and microscopic findings of atheroma resembled those found in man. The evidence from this study suggests that the activity of the clotting system is related to the development of atherosclerosis in swine, and the type of fat fed is an important factor in determining these changes.

Endocardial Fibroelastosis: A Summary of the Literature and a Review of 24 New Cases. W. F. McCormick. South. M. J. 51:1232-1240 (Oct.) 1958 [Birmingham, Ala.].

Of 11,347 autopsies performed at the institute of pathology of the University of Tennessee College of Medicine and at the Baptist Memorial Hospital in Memphis between 1947 and 1957, a diagnosis of endocardial fibroelastosis was made in 24. This represents an incidence of about 0.2% of all the autopsies. There were 15 cases in which no other lesion was found in the heart, and these were classified as primary. The remaining 9 cases occurred in association with such congenital cardiovascular defects as interventricular septal defect (4 cases), patent ductus arteriosus (1 case), patent foramen ovale (3 cases), and infantile coarctation of the aorta (2 cases). These 9 cases were classified as secondary. Of the 24 patients with endocardial fibroelastosis, 13 were males and 11 were females, substantiating the findings of other workers that there is no real sex difference. There were 16 white and 8 Negro patients. Since the percentage of Negro patients in the total autopsy population outnumbered the white, this difference may be a real one, although most other workers did not find any racial difference. The average age of the patients with primary endocardial fibroelastosis was 10 months, and that of those with the secondary condition was 14 months. These figures are in agreement with those found in the literature.

Cyanosis was observed in 7 of the 15 patients with primary endocardial fibroelastosis but in only 3 of the 9 with the secondary condition. Murmurs were heard in only 2 of the 15 patients, and in 7 of the 9 patients. The absence of murmurs in the primary form seems to be of real value in the clinical diagnosis. Murmurs found in the secondary form are undoubtedly due, in most of these patients, to the other anomaly present, such as a septal defect. Cardiac hypertrophy was a constant feature in both groups. This enlargement was often extreme, with hearts found up to 5 times their normal size. A clinical diagnosis of primary endocardial fibroelastosis was made in 2 patients, and a pericardial poudrage with U.S.P. talc was done. Both of these patients lived only a short time. A clinical impression of endocardial fibroelastosis was correct in 2 other patients with the primary form of the condition. A third patient who had the secondary form of the condition underwent surgical correction for the associated interventricular septal defect and died on the second postoperative day.

The gross anatomic findings in primary endocardial fibroelastosis were remarkably constant. Cardiac hypertrophy was always present. The left ventricle was involved in almost all the patients, often without involvement of any other chamber. The endocardium was grossly thickened, often measuring 1 to 3 mm. in thickness. The heart valves were involved infrequently in this series, but other workers have reported involvement in about 50% of all the patients. Unlike some of the reports in the literature, secondary endocardial fibroelastosis was not seen in most cases of congenital heart disease in this autopsy population. This may be due to a more rigid selection of cases on the part of the author. Only those cases with significant gross evidence of endocardial thickening were used in this study. Microscopically, the absence of increased glycogen in the myocardium was a constant finding. The chief finding was thickening of the endocardium. It has been suggested that this thickening is due to deposition of fibrin from the blood and gradual incorporation of this fibrin into the endocardium. The evidence for this, based chiefly on electromicroscopic observations, is inconclusive at this time. Attempts by the author and by other workers to stain fibrin selectively have failed.

RADIOLOGY

Visualization of the Coronary Circulation by Occlusion Aortography: A Practical Method. C. T. Dotter and L. H. Frische. Radiology 71:502-524 (Oct.) 1958 [Syracuse, N. Y.].

The authors describe a technique for coronary angiography, which proved safe and reliable in dogs. The new technique of coronary arteriography is an occlusion aortography, which makes use of a special double-lumen balloon catheter to inject a small quantity of contrast agent (Thorotrast) close to the orifices of the coronary arteries during brief but total occlusion of the aorta just peripheral to the injection site. Since all the contrast agent enters the coronary arteries, maximum efficiency is achieved. Experimental observations during more than 500 complete aortic occlusions and 350 injections in 51 dogs support the belief that this technique is safe and reliable.

The increased efficiency of occlusion aortography for coronary visualization allows the use of small volumes of relatively dilute agents in obtaining improved visualization routinely instead of sporadically. By comparison, thoracic aortography constitutes a less efficient and more hazardous method for coronary visualization in that it involves the relatively uncontrolled intra-aortic injection of 10

to 20 times the needed amount of a type of contrast substance which has caused over 200 reported fatalities. The use of occlusion catheters in gaining controlled access to the cardiovascular system promises to open up many unexplored clinical and experimental possibilities, examples of which are (*a*) new techniques for cardiovascular visualization, (*b*) elective controlled cardiac arrest in the intact subject for purposes such as cardiovascular visualization, and (*c*) total cardiopulmonary bypass as an emergency therapeutic measure in the intact patient.

PUBLIC HEALTH

Report of an Outbreak of Febrile Illness with Pharyngeal Lesions and Exanthem: Toronto, Summer 1957—Isolation of Group A Coxsackie Virus. C. R. Robinson, F. W. Doane and A. J. Rhodes. Canad. M. A. J. **79**:615-621 (Oct. 15) 1958 [Toronto].

The authors report on 47 children, between the ages of less than 6 months and 9 years, and on 13 adults, of an average age of 31 years, who were affected by a febrile illness with pharyngeal lesions and a vesicular rash in a suburb of Toronto in June and July, 1957. The distinctive triad of fever, ulcerative lesions of the fauces and the mouth, and a bullous eruption arising from a macular rash is considered to constitute a new clinical syndrome. The disease was mild in each of the 60 patients, and admission to hospital was not necessary. There were no sequelae. A total of 27 families was affected. Clinical disease occurred in 60 (52%) of the 115 members of these families. The illness spread progressively through adjacent blocks of houses and also from one family to another. The incidence of illness was highest in children of the 1-to-9-year age group (42 of the 47 children), and it was considered that they introduced the illness into the family groups. The high incidence of illness in this age group is explained by reason of the close contact of the children at play and in particular through use of small portable swimming pools.

Attempts at virus isolation were made by the inoculation of specimens obtained from 31 patients into monkey kidney-tissue and into suckling mice; virus was isolated from 22 of these patients (71%). The virus showed some serologic relationship to Coxsackie virus, group A, type 16. The isolation of this virus from 22 (79%) of 27 stool specimens obtained from these patients suggested a causal relationship between it and the clinical illness described. This suggestion was supported by the demonstration of a specific antibody response to the related Coxsackie virus, group A, type 16, in 3 patients, by the temporal relationship of virus isolation to the clinical syndrome in one patient, and by the absence of illness or virus isolation elsewhere in the population of the city of Toronto at the time of the outbreak and during the summer of 1957.

Observations on the Excretion of Type 1 Poliovirus from Cases and Their Contacts. L. A. Hatch, K. E. A. Hughes and J. N. Pilfold. Am. J. M. Sc. **236**:419-424 (Oct.) 1958 [Philadelphia].

Many views on the application of quarantine measures for the prevention of poliomyelitis have been based on the recommendation of the World Health Organization (1954): "Children with familial or intimate exposure should be confined to their homes for 21 days. Adults need not be confined, but they should refrain from association with children other than their own and should avoid intimate contact with adults." Other workers described findings at variance with this recommendation. The authors report that at the Public Health Laboratory in Portsmouth, England, isolation of poliomyelitis virus was attempted in feces and throat swabs obtained from poliomyelitis patients and their contacts. This material was tested in HeLa cells. When the virus was isolated from feces, its identity was established by neutralization tests with monospecific hyperimmune monkey serums prepared from each of the 3 types of poliomyelitis virus. In many instances it was possible to examine repeated specimens of feces, collected at approximately weekly intervals. From July, 1956, until the end of 1957, type 1 poliomyelitis virus was isolated from 2 or more specimens of feces from each of 93 patients who were considered clinically to have nonparalytic or paralytic poliomyelitis, and also from 97 healthy contacts. From the results obtained it appears that half of the patients with poliomyelitis would be expected to excrete virus for about 3 weeks after the onset of their illness and that only after 8 weeks would this proportion fall to less than 10%. Half of the healthy contacts can be expected to excrete virus for about 5 weeks after the onset of illness in the index case, and the proportion would not fall below 10% until 8 to 10 weeks have elapsed.

These findings suggest that the rate of clearance of poliomyelitis virus from the stools follows an exponential curve. HeLa cells are generally regarded as being slightly less sensitive than other tissue cells in the detection of poliomyelitis virus in feces, and it may well be that these figures understate the length of period of excretion of poliomyelitis virus. This small series, however, indicates that the potential dangers arising out of the presence of poliomyelitis virus in the stools of a large proportion of convalescent patients and home contacts may persist longer than is generally recognized, though, in the absence of information on the amount of virus excreted, it would be unjustifiable to assume that the danger remains the same throughout the period of excretion.

BOOK REVIEWS

The Acute Abdomen. By William Requarth, M.D., Clinical Assistant Professor of Surgery, University of Illinois College of Medicine, Chicago. Foreword by Warren H. Cole, M.D. [Formerly titled Diagnosis of Acute Abdominal Pain.] Second edition. Cloth. $6.50. Pp. 313, with 89 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

This book is designed primarily to assist young surgeons and medical students in the diagnostic problems that acute disorders of the abdomen may entail. It is proper then that detailed instructions relative to the examination of the abdomen be included. The value of the history as it relates to the patient's abdominal complaint is emphasized. It is in this area in particular that the depth of the author's experience becomes evident. Much of the clinical symptomatology has been tabulated to compare the merits of various signs and symptoms in relation to different abdominal diseases. Intestinal obstruction and its causes, diagnosis, and treatment, is thoroughly discussed, and excellent illustrations are presented. The latter half of the book gives the details of those diseases in which immediate operation is required, those in which operation can be delayed, and those in which it is contraindicated. In addition, traumatic wounds of the abdomen, congenital disorders, and the management of gastrointestinal hemorrhage constitute separate chapters. The principal assets of this book are its concise presentation and its small size. Its chief usefulness should be in emergency wards and surgical floors—wherever students, interns, and residents are in training. It should also be of benefit to physicians in general practice.

Roentgen-Diagnostics: Progress Volume I. By H. R. Schinz, R. Glauner, and E. Uehlinger. With collaboration of W. E. Beansch and others. Translated from German by James T. Case, M.D., D.M.R.E. [Rontgendiagnostik Ergebnisse 1952-1956, published by Georg Thieme Verlag.] Cloth. $35. Pp. 623, with 545 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

This magnificently printed, beautifully illustrated volume may be considered a companion to the previously published four-volume "Roentgen Diagnostics," by Schinz and co-workers. It is made up of a series of concise articles and monographs that thoroughly cover the progress in diagnostic roentgenology from 1952 through 1956, with the bibliography including papers through 1957. Most of the volume is devoted to articles on the use of contrast substances, particularly the various forms of angiography. Many other subjects are discussed. The short chapter on evaluation of cardiac function in the adult by roentgenographic means and the chapter on direct and differential diagnosis of diseases of the pulmonary stroma are outstanding. All of the sections are as thorough and informative as is consistent with the space available. This volume is a worthy addition to the reference textbooks on diagnostic roentgenology and, in its own right, should prove valuable. For those fortunate owners of "Roentgen Diagnostics" it is almost a necessity, as it expands and supplements that work to perfection. The editors, authors, and translators have, as before, done a fine job. It is hoped that in the future the lag between translation and publication can be shortened.

The Cervical Syndrome. By Ruth Jackson, B.A., M.D., F.A.C.S., Clinical Assistant Professor of Orthopaedic Surgery, University of Texas, Southwestern Medical School, Dallas. Publication number 334, American Lecture Series, monograph in Bannerstone Division of American Lectures in Orthopaedic Surgery. Edited by Charles Weer Goff, M.D., Associate Clinical Professor of Orthopaedic Surgery and Lecturer in Anatomy, Yale University School of Medicine, New Haven, Conn. Second edition. Cloth. $6.50. Pp. 197, with 90 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This book describes and differentiates between the pathological conditions in the cervical spine which may produce headache and pain or stiffness of the neck and shoulder. The structure and the lesions of the cervical spine, with particular reference to the posterior-lateral facets described first by Von Luschka, are graphically described and illustrated. The mechanism and significance of the whiplash injury are thoroughly discussed. There are 40 new illustrations, including colored drawings of the anatomy of the cervical spine. This valuable book should be useful to the general practitioner, orthopedist, and neurosurgeon.

Ophthalmic Plastic Surgery. By Sidney A. Fox, M.S. (Ophth.), M.D., F.A.C.S., Associate Clinical Professor of Ophthalmology, New York University Post-Graduate Medical School, New York. Second edition. Cloth. $15. Pp. 324, with 149 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

This edition, appearing five years after the first, emphasizes pictures and illustrations rather than written explanations. The drawings are simple and clear. Only that part of the anatomy of the brow

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and lids that pertains to plastic surgery is included. One of the highlights of the book is the chapter on ptosis, in which the author does not outline innumerable procedures to confuse the reader but carefully depicts a few procedures of each type in detail with some modifications of his own. In other words, this is not an encyclopedia but an ophthalmic plastic surgery book based on surgical procedures performed by the author personally. Because of the tremendous increase in traumatic accidents involving the face and eyes, this book assumes increasing importance in ophthalmic practice. It behooves all ophthalmic surgeons to familiarize themselves with its contents.

Electrocardiography. By Michael Bernreiter, M.D., F.A.C.P., Assistant Clinical Professor of Medicine, University of Kansas Medical School, Kansas City. Cloth. $5. Pp. 134, with 92 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 4865 Western Ave., Montreal, Canada; Pitman Medical Publishing Company, Ltd., 45 New Oxford St., London, W. C. 1, England, 1958.

This book was designed for the beginning student in electrocardiography. Its purpose is to clarify the basic principles involved in the study of electrocardiograms and their clinical interpretation. The author has done a commendable job in explaining the physiology and electrophysics in both normal and abnormal electrocardiograms by liberal use of schematic illustrations. After establishing the foundation of the electrical phenomena of electrocardiography, their clinical application is discussed. This has been documented with good illustrative electrocardiographic tracings. The author has covered arrhythmias, heart block, hypertrophy, currents of ischemia, and changes resulting from necrosis of the myocardium, plus the characteristic patterns of the various forms of electrolyte imbalance. Also discussed are the effects of digitalis and quinidine and the significance of alterations in the Q-T interval. The author spent much time in the planning and illustration of the material presented. He also avoided long and technical discussion of controversial phases of electrocardiography. Any reader who devotes time to this subject should be amply rewarded by being able to read competently most of the electrocardiograms he sees.

Pediatric Surgery. By Orvar Swenson, Professor of Pediatric Surgery, Tufts University School of Medicine, Boston. Foreword by William E. Ladd. Cloth. $20. Pp. 740, with 980 illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1958.

This book is an up-to-date, easily readable, and comprehensive new work that covers essentially all aspects of pediatric surgery. Its author is an authority in the field; his work on megacolon is especially noteworthy. This book will undoubtedly be regarded as a standard textbook on this subject. The volume is beautifully illustrated with diagrams, photographs, and roentgenograms of most of the subjects covered. There are, in addition, numerous tables, formulas, and charts covering most aspects of pediatric surgical care. Most of the discussions include anatomic and diagnostic considerations and details of preoperative care, anesthesia, operative technique, postoperative management, and effectiveness of the management. The details of a number of relatively minor surgical manipulations, such as bronchoscopy, cystoscopy, insertion of a chest tube, and sigmoidoscopy, are aspects of this book especially valuable for the intern or resident. The operative techniques of the larger procedures are also presented in step-wise fashion and, again, with excellent illustrations. The chapters dealing with megacolon and with urologic problems are especially well written. Chapters on the management of congenital malformations of the head and neck, burns, fractures, and surgical lesions of the skin and extremities are also presented. A relatively new clinical entity, chalasia, is also discussed. This book should appeal as much to the undergraduate student of medicine as to the intern, resident, and surgeon.

The Care of the Patient in Surgery Including Techniques. By Edythe Louise Alexander, R.N., B.S., M.A., Director of Nursing Service and Principal of School of Nursing, Lutheran Medical Center, Brooklyn. [Previous editions titled Operating Room Technique.] Third edition. Cloth. $12.75. Pp. 840, with 555 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

It is indeed rare to visit an operating suite that does not have a copy of Alexander's now classic work. This new edition is excellent and a worthy successor to its predecessors. It is concerned primarily with operating room procedures and armamentarium. Although it is beamed to nurses, it might be of great value to the young surgeon as a general review of procedures and an orientation in the responsibilities of the operating room staff. The general format of the book has not been changed, although there has been much revision reflecting changes in surgical procedures in the past nine years. The chapter on neurosurgery is especially well written. That on cardiovascular operations considers the established procedures being performed in most hospitals today but does not discuss the highly technical procedures requiring bypass and oxygenating equipment. The author is to be complimented on writing a concise informative textbook. It can be recommended highly to all persons interested in surgery and especially to those who provide and maintain the asepsis so necessary to the success of any operation.

QUESTIONS AND ANSWERS

ASIAN INFLUENZA

To the Editor:—*How effective is the Asian influenza vaccine? In the United States in the 1957-1958 epidemic, how many persons suspected of having this disease had blood tests made to confirm the diagnosis? Of these tests, how many gave positive results?*

Victor W. Higgins, M.D., Essex, Conn.

Answer.—In the summer of 1957, as soon as influenza vaccines of desired potency became available in sufficient quantities, a number of studies were conducted to assess their effectiveness against the impending epidemic of Asian influenza. The results of some of these studies are summarized in a paper by Davenport (*Pub. Health Rep.* **73**:133, 1958). The estimated effectiveness of the monovalent vaccines ranged in these series between 42% in a study by Culver and Lennette and 77% in a study by Rose and associates. The effectiveness of the vaccine in both instances was estimated by comparing the attack rates from respiratory disease between vaccinated persons and suitable control groups. The substantial difference in protection in these two studies can be explained to a large extent by the differences in the antigenic potency of the vaccines used (250 and 750 CCA units respectively). The effectiveness of the vaccine is also discussed in papers by Hilleman and co-workers (*J. A. M. A.* **166**:1134-1140 [March 8] 1958) and Meiklejohn (*Am. J. Hyg.* **67**:237, 1958). On a nationwide basis, no data are available regarding how many persons with suspected disease had blood tests to confirm the diagnosis during the 1957-1958 epidemic or how many of these tests gave positive results. In one study of an epidemic of Asian influenza (Carey and co-workers, *J. A. M. A.* **167**:1459-1463 [July 19] 1958), serologic studies, in addition to a retrospective questionnaire survey, were carried out among 428 school children; these revealed an attack rate of 65% for subjective "flu," confirmed serologically in 87%.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

EQUALIZATION OF LIMB DISCREPANCY

To the Editor:—*How can equality of leg length best be obtained when there is an 8-in. difference? A 14-year-old boy has a short leg due to trophic disturbances and loss of bone substance associated with avulsion of soft parts. A tree fell on him eight years ago. The femoral neck is in valgus, and in the subtrochanteric level there is a malunion deformity of the shaft, producing an anterolateral curvature. At this same level there was loss of musculature, with the result that the bone is not normally buried in the soft tissue. This area might prove to be vulnerable to irritation from any prosthetic device which might be applied to the thigh. Most of the shortening is from lack of femoral growth, but the tibia has also failed to grow normally. On the affected leg, the knee is at about the level of the junction of middle and lower thirds of the normal thigh. The boy has no pain. By the use of a high cork lift, a pelvic tilt, and a short leg limp, the patient walks without brace, crutch, or cane but with an objectionable gait. Could any prosthetic device be applied without amputation?*

Robert C. Keys, M.D., South Norwalk, Conn.

Answer.—Eight inches of limb discrepancy, if not accounted for by loss of bone substance, probably is due to premature closure of growth of the major epiphysial disks in the knee. This may occur directly from trauma or secondarily from prolonged disability of the limb. The deformity at the hip may account for some of the apparent shortening of the limb. The femoral neck is described as being in valgus. In view of the lateral bowing deformity in the subtrochanteric region, it would seem more likely that the neck is in marked varus. If such is the case, its correction by subtrochanteric osteotomy may be of value in reducing the limp and in giving some functional lengthening of the limb. No statement is made as to the condition of the skin covering the traumatized region. It may be that some plastic procedure on the soft parts would be advisable. Roentgenograms of the knee region should be made to determine if the epiphyses have closed. If they are still growing, amputation should be postponed until growth is completed. If the true shortening of the limb amounts to 8 in., equalization of the limbs by surgical lengthening and short-

ening of the opposite side should not be attempted. The discrepancy in length will have to be made up by some sort of prosthesis. Commonly used is an elevated platform shoe, but this is awkward and cosmetically unsatisfactory. A prosthetic device which laces on to the lower leg and contains an elevation which permits the use of the foot in marked equinus might be of service, but it, too, is cumbersome. Amputation may be most satisfactory from a cosmetic and functional standpoint; amputation above the knee may be desirable because of the great discrepancy in the level of the knee joints. This would give a thigh stump with a mechanical knee at the same level as on the normal side. Cosmetically it would be very satisfactory. Amputation below the knee would preserve the normal knee joint, but the prosthesis would have to make up for the length discrepancy and might be awkward in use. An end-bearing stump, such as with the Syme's amputation could be constructed and fitted satisfactorily. The prosthesis would encompass the lower leg, and equalization of the leg would have to be obtained by extension of the prosthesis. Cosmetically this would not be too satisfactory and, since it is not a standard limb, would be costly in its replacement over the years. Thus, any existing deformity should be corrected and any required soft parts plastic procedure done, and decision as to amputation and prosthesis should be made in consultation with a large amputation service where the experience of a limb manufacturer and a surgeon can be correlated.

CEREBRAL ANEURYSM IN CHILDREN

To the Editor:—*In children with ruptured cerebral aneurysm near the circle of Willis, what are the chances of recurrence of the bleeding in later life if ligation or obliteration cannot be carried out? Is it considered necessary to limit a child's activities for an indefinite period? For how long a time should the child be at bed rest after an attack?*

Ruskin King, M.D., Savannah, Ga.

Answer.—The fate of an aneurysm is difficult to predict because there are so many variables. Generally, the aneurysm does not give rise to symptoms until puberty or early adult life. Since the congenital defect is a weakness of the blood vessel wall, eventually, in a large percentage, it will rupture. Each episode of subarachnoid hemorrhage sharply increases the mortality. Therefore, all measures to preserve life and to diagnose and treat the aneurysm should be attempted. After the onset of the hemorrhage, the patient should remain in bed until such symptoms as headaches and nuchal rigidity disappear. The period of time is generally a minimum of four weeks. Cerebral angiography is an invaluable diagnostic method which is well tolerated by children. If the aneurysm cannot be ligated or trapped surgically, the child should be allowed to follow an essentially normal pattern of life, with the exception of limitation of physical exertion.

VAGINAL REPAIR AND CESAREAN SECTION

To the Editor:—*Does vaginal repair warrant a cesarean section in subsequent pregnancies?*

Nerio W. Pioppi, M.D., Southbridge, Mass.

Answer.—An answer to this question with an unqualified "yes" or "no" would be an incomplete one. The extensive Fothergill type of vaginal repair operation was predicated with the probability that subsequent vaginal delivery would be routine. Certainly every obstetrician can recall an instance in which delivery with hysterectomy was deemed advisable. For example, one patient had a successful closure of a vesicovaginal fistula after two previous attempts had failed. An orthodox anterior and posterior colporrhaphy seldom warrants cesarean section in subsequent pregnancies.

BLOOD EXAMINATIONS WITH OXALATED BLOOD

To the Editor:—*The answer given on the question about blood examinations with oxalated blood, which appeared in* The Journal, *Nov. 15, 1958, page 1593, is somewhat at variance with statements made by other authorities in the field. The questioner indicated that an oxalate mixture was used as the anticoagulant in a vacuum tube. The two major suppliers of vacuum tubes supply only one oxalate mixture, and that is a combination of ammonium and potassium oxalate. Wintrobe (Clinical Hematology, ed. 4, Philadelphia, Lea & Febiger, 1956, chap. 8) states, "We have found a mixture of dry ammonium and potassium oxalate to be very satisfactory." In the same chapter, he states, "It has been repeatedly shown that there is no difference in counts made on venous blood as compared with capillary blood, if proper precautions to secure a freely flowing sample are observed in each instance." Although none of the hospitals with which I am associated use vacuum tubes, I know of several reputable hospital laboratories that routinely use these, with balanced or double oxalate as the anticoagulate, for hematological procedures and find them quite satisfactory. The oxalate does alter the morphology of the leukocytes in the stained smears.*

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